MALARIA IN INDIA

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MALARIA IN INDIA

BY

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TO THE MEMORY OF THE LATE

FRANK LLOYD, Esq.

OF

Coombe House, Croydon

PREFACE

THE present volume has grown out of my *Prophylaxis of Malaria in India* (1910) which, revised, enlarged, illustrated and brought up to date, is incorporated with it. While all the more important aspects of the subject of malaria in India have been dealt with, the main effort throughout has been concentrated on the practical side of prevention in communities and in the individual. It is possible that in some instances, such as the sections on PREVENTION OF MALARIA IN TOWNS AND IN CANTONMENTS, the methods of prevention detailed are unnecessarily elaborate. This, indeed, was a criticism made against the earlier book, but with it I do not agree. The several measures described in each case give a choice of methods; towns and cantonments, from the point of view of the malaria sanitarian, differ from one another very much; in one drainage is the main operation called for, in another screening of houses, in a third fish control, in yet another quinine (or cinchona febrifuge) treatment of the infected, although in most instances all of these, and perhaps other, measures may be required.

I would invite attention to the sections on the ECONOMIC PROBLEMS CONNECTED WITH QUININE IN INDIA and ECONOMIC AND SOCIOLOGICAL QUESTIONS CONNECTED WITH MALARIA IN INDIA. An attempt has been made to compare the therapeutic merits of quinine (and other alkaloids of cinchona bark) and cinchona febrifuge, and the question of a large increase in the production of cinchona febrifuge, at such a price as to make it available to the masses, has been considered. Both problems are highly technical and complicated, but no work dealing seriously with the malaria of India can evade them. I have indicated the lines upon which, in my opinion, further inquiry should be undertaken before a final solution is arrived at. In any circumstances, for some years to come, the use of these drugs can have only a partial effect on the reduction of malaria in India, as at the present time not more than 10 to 15 per cent. of the cases of malarial infection occurring there are treated by quinine or cinchona febrifuge, and it will be many years before the latter drug can be manufactured at a price that the masses can meet. I have advocated State control of the cinchona febrifuge industry, including the distribution of the drug, as the best method of stabilising the cost of it and preventing its sophistication. It is deserving of consideration whether quinine should be embraced in this control.

I have also deemed it obligatory to deal with the bearings of the economic and sociological conditions of the masses of India on the reduction of malaria; frankness and conviction demand this, as these subjects are probably more important than the preventive measures detailed in the text. These measures, if properly carried out, can very materially reduce the malaria among the educated classes living in satisfactory economic, hygienic and social conditions, but they are at present beyond the education, comprehension and the means of the *unaided* rural masses; these masses preponderate incomparably over the well-to-do.

In order to bring the book quite up to date I have included in Appendix VI

some additional information on malaria published while this volume was passing through the press.

I gratefully acknowledge the help given me by Prof. J. W. W. STEPHENS, M.D., F.R.S., and Lt.-Col. CLAYTON LANE, M.D., I.M.S., in preparing this volume; their many valuable suggestions have been incorporated in the book. Lt.-Col. CLAYTON LANE has, in addition, aided in the revision of the work, and seen it through the press. Indeed, without the generous assistance of these two distinguished malariologists it is doubtful whether this edition would have been published.

I have also to thank several authors and publishers for permission to use plates and other illustrations from their works. These include Prof. J. W. W. STEPHENS and Lt.-Col. S. R. CHRISTOPHERS'S *Practical Study of Malaria* (Liverpool University Press); Dr. P. H. MANSON-BAHR, D.S.O., M.D., F.R.C.P., Editor of Sir PATRICK MANSON'S *Tropical Diseases* (Cassell & Co.), Drs. C. W. DANIELS and H. B. NEWHAM'S *Laboratory Studies in Tropical Medicine*, Lt.-Col. S. P. JAMES'S *Malaria at Home and Abroad* (Messrs. Bale, Sons & Danielsson); Sir MALCOLM WATSON'S *Prevention of Malaria in the Federated Malay States* (Mr. John Murray); Lt.-Cols. S. P. JAMES and GLEN LISTON'S *Anopheline Mosquitoes of India* (Thacker, Spink & Co., Calcutta); Lt.-Col. W. BYAM and Major R. G. ARCHIBALD'S *Practice of Medicine in the Tropics* (Oxford Medical Publications), and Mr. W. E. HARDENBURG'S *Mosquito Eradication* (McGraw-Hill Book Company, Inc., New York). The plates, plans, photographs and other forms of illustration are fully acknowledged in the body of the book.

I am specially indebted to Lt.-Col. S. R. CHRISTOPHERS, C.I.E., O.B.E., F.R.S., I.M.S., for creating the Malaria Map of India; it is the first of its kind constructed and was prepared for this volume. I have likewise to thank Messrs. Howard & Sons for the blocks of the plants *Cinchona succirubra* and *C. succirubra* × *C. ledgeriana*; they have also assisted me much in dealing with the subject of quinine in India.

I have to thank my wife for making all the original sketches, plans and illustrations, and for much help in various ways in the output of the book.

I have obtained a considerable amount of valuable information from the following medical periodicals: *The Lancet*, *The British Medical Journal*, *Tropical Diseases Bulletin*, *Annals of Tropical Medicine and Parasitology* and *The Indian Medical Gazette*.

It is due to myself to state that during the War I lost two large boxes containing most of the MSS. of the present volume, together with many hundreds of maps, plans, sketches, original illustrations and photographs collected between the years 1909 and 1918 while making many malaria surveys and the reports connected with them. Most of these are well known in the cantonments and districts with which they are connected; they were always submitted in manuscript; only in the case of Burma were they subsequently printed. All efforts to obtain copies have failed. This explains the delay in publishing the present volume, and the reason for using so many borrowed illustrations.

P. HEHIR.

WESTWARD HO! DEVON.
July 1927.

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MALARIA IN INDIA

SHORT HISTORY OF MALARIA

What is Malaria?—The term *Malaria* (It. *mala* bad, *aria* air) was first applied about the year 1712 to a group of fevers having certain special characteristics. The name is unfortunate and ætiologically incorrect. At the time of its introduction it was believed that *miasmata* gave rise to malarial diseases of all kinds; and though this word perpetuates an obsolete view, we are obliged from its antiquity to retain it. It has been ineradicably established in our terminology and its meaning is universally understood. The term Malaria is also applied to the special causes of malarial diseases, and to the combination of conditions that bring those causes into operation.

Malaria has probably been in existence since the infancy of the human race. The ancient Egyptians possessed some knowledge of malarial fevers. It is said that the word A A T, which is found among the inscriptions of the temple of Denderah, referred to a disease, doubtless malaria, which recurred yearly at the same season. More than 1,000 years B.C., malarial diseases were mentioned in the *Orphic Poems*. Some of the early plagues mentioned in the Bible, and the vast epidemics which assailed the Assyrian and Babylonian armies, were possibly malarial. According to HERODOTUS, the fishermen on the Nile used their fishing nets to prevent the attacks of mosquitoes. The *Iliad* of HOMER (eighth century B.C.) and the *Wasps* of ARISTOPHANES (fifth century B.C.) contain allusions to malarial fevers, and HIPPOCRATES (fifth century B.C.) gave a fairly complete description of these diseases. HIPPOCRATES differentiated malarial from continuous fevers, observed the periodicity of the paroxysms, and divided these fevers into quotidian, tertian and quartan. Ancient Hindoo medical writers describe in their peculiar way the intermittent and remittent malarial fevers. The "fevers" said to be spread by mosquitoes in the *Charaka-Samhita* are probably malarial. CELSUS (first century A.D.) described practically all the forms of malarial fever recognised to-day, including the two types of tertian. CATO, CICERO, VARRO, LIVY and other writers of ancient Rome give positive evidence of an acquaintance with malarial diseases. The Arab physician RHAZES (fifteenth century) was familiar with and wrote about malarial fevers. During the darkness and superstition of the Middle Ages no additions were made to our knowledge of malaria, and it was not until the middle of the seventeenth century that the first real stage of the history of malaria was entered upon.

MECKEL (1847) declared that the dark colour of internal organs in malaria was due to pigment. VIRCHOW (1848) stated that this pigment was contained in cells. KELSCH (1875) noted pigmented bodies in malarial blood and later (1880) concluded that these pigmented cells (melaniferous leucocytes) were characteristic of malaria and of diagnostic value.

Three chief discoveries in connexion with malaria.—In the history of malaria there have been three dominating discoveries:

(1) That of the specific action of cinchona bark on malarial fevers in the seventeenth century.

(2) That of malaria parasites in the blood by LAVERAN in November, 1880.

(3) That by RONALD ROSS that malaria parasites of birds become sporozoites in the salivary glands of mosquitoes.

(1) **Discovery of cinchona bark.**—Cinchona bark was introduced from Peru into Spain by the Viceroy del Chinchon and his physician Juan del Vego in 1640. It was largely used under the name "Jesuits' bark," because used by the Jesuits of Peruvian monasteries in the treatment of certain fevers. It had antecedently been long used by the indigenous people for the same purpose. In India it was first employed by Dr. BOGUE in Calcutta during the malaria epidemic of 1657. JAMES LIND used it extensively in Lower Bengal in 1765. He says: "In the proper administration of the bark the cure of agues may be said to entirely consist." He also used "bark" as a prophylactic. WILLIAM HUNTER (1804) treated malarial fevers with drachm doses of bark every two hours during remissions. JOHN CLARK (1809) said that "the cure must entirely depend upon giving Peruvian bark in as large doses as the patient's stomach will bear, without having any regard to the remissions or exacerbations of the fever."[1]

Anterior to the discovery of cinchona bark and its use in the treatment of fevers, malarial and other fevers were mixed up in the most confused way. This first real period in the history of malaria embraces (*a*) recognition of the action of cinchona bark in malarial fevers, and (*b*) the therapeutical specific division of fevers into the two classes—those that are curable by it and those that are not. In this latter work we are specially indebted to MORTON, TORTI and SYDENHAM. On this foundation Torti wrote his classic account of malarial diseases. His descriptions of the clinical manifestations of malaria excelled those of all previous writers, and remain up to the present a monumental record of his clinical and scientific acumen.

In England, before quinine was extracted from cinchona bark, paroxysms were sometimes treated by giving the patient an ounce of bark infused in a pint of hot beer; he was put into a warmed bed, and remained there until the sweating stage was over.

The extraction of the alkaloid *quinina* from cinchona bark by the two chemists CAVENTOU and PELLETIER in 1820 marked another phase in the history of anti-malarial therapeutics. Quinine was first used in India in Bombay in 1826, but did not come into general use for another quarter of a century.

(2) **Discovery of malaria parasites by Laveran.**—The second real epoch in the history of malaria was the discovery by LAVERAN of protozoal organisms in fresh blood in cases of malarial fever in Algeria in November, 1880. He began his inquiry by investigating the nature of the pigment that occurs in malaria. He examined the blood of patients suffering from malaria and completed these observations in the dead body. He recognised that there were pigment-containing bodies in malaria other than leucocytes; and first conjectured, and subsequently proved, that these bodies were the parasites of malaria. Among other discoveries he described the long motile filaments of the flagellated microgametocyte, which he had watched, making their exit from the pigmented cells previously described by MECKEL and others. The eruption of flagella was observed in crescents, which, because of the absence of movement, had been considered inanimate. LAVERAN's discovery met with considerable opposi-

[1] SIR LEONARD ROGERS, *Fevers of the Tropics*, p. 2.

tion, even after its confirmation in 1882 by RICHARD and its corroboration by CELLI, GRASSI, GOLGI, BIGNAMI, BASTIANELLI, MARCHIAFAVA and others. Several authorities declared the actual parasites to be the degeneration products of red cells. Much investigation and research carried out about this time showed that many animals harboured in their blood parasites similar to the malaria parasites in man.

GERHARDT (1884) proved that malarial fevers could be transmitted direct from man to man by the inoculation of the blood of persons suffering from malarial fever into those that were healthy. GOLGI, MARCHIAFAVA and CELLI first distinguished the different species of malaria parasites. They demonstrated that a particular type of malarial fever could be produced by injecting the blood of a patient suffering from that type into a healthy man. GOLGI discovered that the commencement of the malarial paroxysm coincides with the sporulation of the parasite. In 1885 he confirmed LAVERAN's work, and added largely to our knowledge of malaria. He formulated a series of laws which may be looked upon as classical. These are—

(i) Malaria parasites multiply in the blood by simultaneous sporulation.
(ii) Fever begins when the spores are liberated.
(iii) Different varieties of malaria parasites exist.

He showed that the cycle of quartan was seventy-two hours, of simple tertian forty-eight hours. He had heard of "crescents" but had not seen them, and inferred that they were connected with a different variety of fever.

(iv) Certain forms do not produce spores. These are now known to be *gametocytes*.

Shortly afterwards, MARCHIAFAVA, CELLI and BIGNAMI worked at the æstivo-autumnal fevers of Italy. They demonstrated the characteristics of the malignant tertian parasite, and showed that its sporulating forms are seldom found in the peripheral blood.

(3) **Discovery by Sir Ronald Ross that malaria parasites of birds become sporozoites in the salivary glands of mosquitoes.**—The real epoch-making step towards a scientific elucidation of the epidemiology and endemiology of malaria was taken by Sir RONALD ROSS, who demonstrated the development of the sexual forms of malaria parasites in the stomach of the mosquito. This was suggested by epidemiological facts and certain phases in the life-history of the parasite indicating the necessity for alternation of generations together with a change of host. Sir PATRICK MANSON, having, in 1884, traced the earlier stages of the development of the *Microfilaria bancrofti* to its infective form in the thoracic muscles of *Culex fatigans*, argued, in regard to malaria, that mosquitoes rescue the parasites from the human blood vessels by sucking them out, and so offer them opportunity for further development within their bodies. Sir RONALD ROSS proved that MANSON's view was correct. MANSON inferred that the exflagellation observed by LAVERAN was a phase in the life-history of malaria parasites. ROSS showed (1895) that it occurred more readily in the stomach of certain mosquitoes than in ordinary finger-blood preparations (the first evidence in favour of MANSON's hypothesis), and that it did not occur if finger blood were collected under vaseline. In that year MACCALLUM showed that in the avian Halteridium the body corresponding to the flagellum of Plasmodium was the male fertilising element, and MANSON urged on Ross the analogy.

Early in 1898 Ross proved that "if a particular species of mosquito (Culex) be fed on the blood of birds containing a parasite—Proteosoma, nearly allied to that of man—the parasite enters the stomach-wall of the insect, grows and sporulates there, with the production of sporozoites that subsequently enter

the salivary glands of the insect."[1] In the same year he definitely incriminated anopheline mosquitoes as the transmitting agents of human malaria. He showed that only particular species of mosquitoes could carry avian malaria parasites from one bird to another. Further, that these very mosquitoes which carried Proteosoma from bird to bird could not carry Halteridium, nor could they carry malaria parasites from man to man. Having proved that mosquitoes carried avian malaria parasites, it was a short step to assume that they could carry human malaria parasites. But his orders to proceed to Assam and investigate kala-azar prevented his making that single experiment with Anopheles and crescents which would have proved the matter.

Ross's observations on bird malaria were soon confirmed and extended by several Italians, and by DANIELS and R. KOCH. MANSON, GRASSI and others, by applying Ross's observations on bird malaria to man, proved that certain species of anophelines are the definitive hosts of human malaria parasites. GRASSI and BIGNAMI repeated Ross's experiments on birds, but with human malaria parasites on man. The years which have passed have fully confirmed the work done by Ross between August 1895 and August 1898.

Sir RONALD ROSS's work on malaria will continue for all time to be one of the most thrilling examples of scientific industry ever carried out in the hot climate of India.

ROMANOWSKY (1891) introduced his method of staining chromatin, which led to a knowledge of the variation in the distribution of chromatin in cells and a more accurate study of species and cycles of malaria and other protozoal parasites.

C. C. BASS, in 1911, demonstrated that the asexual forms of human malaria parasites could be developed *in vitro*. Besides these outstanding discoveries many other scientific workers have added to our knowledge, and we are now acquainted with most of the important facts connected with malaria. The writer has not the least doubt but that there are other surprising discoveries in store for us, but these will come as additions to our knowledge, and not as fundamental or epochal landmarks.

The genius of Sir PATRICK MANSON and Sir RONALD ROSS altered the whole aspect of the question of the prevention of malaria in the world, and paved the way for the discovery of the causes of other diseases carried to man and animals by insects.

[1] MANSON's *Tropical Diseases*, 8th Ed., p. 1.

PART I

ENDEMIOLOGY, EPIDEMIOLOGY AND ÆTIOLOGY OF MALARIA IN INDIA

PART I

ENDEMIOLOGY, EPIDEMIOLOGY AND ÆTIOLOGY OF MALARIA IN INDIA

IN Part I, after some preliminary remarks, it is proposed to deal with:

A. PREVALENCE OF MALARIA IN INDIA.
B. MORTALITY FROM MALARIA IN INDIA.
C. GEOGRAPHICAL DISTRIBUTION OF MALARIA IN INDIA.
D. CONTRIBUTORY CAUSES OF MALARIA IN INDIA.
E. PREDISPOSING CAUSES OF MALARIA IN INDIA.
F. IMMUNITY TO MALARIA AS MET WITH IN INDIA.
G. RÔLE OF MAN IN THE DISTRIBUTION OF MALARIA IN INDIA.
H. THE HUMAN MALARIA CARRIER.
I. EPIDEMIC MALARIA IN INDIA.
J. THE DEFINITIVE HOSTS OF HUMAN MALARIA PARASITES—INDIAN ANOPHELINI AND THEIR HABITS.
K. THE SPECIFIC CAUSE OF MALARIA—THE MALARIA PARASITES OF MAN IN INDIA.

INTRODUCTION

Malaria has been one of the greatest foes to civilisation; its operations for evil have continued from century to century. Gigantic commercial enterprises, undertaken at different times, have been abandoned on account of the terrible havoc wrought by malaria. All malarial countries are seriously handicapped, and their natural development towards the highest economic, industrial and political efficiency is materially retarded, by their malaria.

Hygienic importance of malaria in India.—It is malaria which is the main cause of the insalubrity of India, and, so long as it continues prevalent, widespread and severe, so long will it sap the vitality of the people. It is, directly or indirectly, one of the chief causes of the high infant mortality, and the main cause of the high sickness-rate, especially among the rural population.

This is no recent observation, for as FLORENCE NIGHTINGALE wrote: "The mortality from malaria in India is a mere trifle compared with the ravage 'fever' commits in sapping the strength and vigour of the people; fever destroys the life of the country—the deaths must be multiplied by fifty or sixty to give the attacks."[1] Again, Sir JOSEPH FAYRER remarked regarding the effects of malaria that "the sun's rays, the heat and other ills, pale into comparative insignificance before its incessant operations against the health and lives of human beings in tropical and tropoidal regions."[2]

Economic importance of malaria in India.—The prevention of malaria is probably one of the most important economic and industrial problems of India. From the vastness of the subject and the numerous complex factors associated with the endemiology of malaria in that country, the difficulties to be encountered in reducing the disease are formidable. Nevertheless, it may with confidence be said that the eradication of malaria from India would, in

[1] *Life and Death in India.*
[2] *Climate and Fevers of India.*

a single generation, convert that country into one of the most prosperous in the world. Unhappily, eradication is not at present a practical proposition; *reduction of malaria is*, and that reduction is an imperial and economic problem of the first importance. The extent to which it can be attempted will depend on the estimate formed of the economic saving which would result from such reduction.

Economic loss caused to the State by malaria in India.—It would be interesting to estimate what malaria costs the State per annum in the various provinces and in the Army in India, were it not that the undertaking would be largely theoretical. Such an estimate would include the original cost of all anti-malarial operations, of hospital accommodation for malaria cases, cost of medical service, feeding, nursing, invaliding, and cost of training recruits to replace mortality and invaliding (direct and indirect) from malaria. In the civil population the many millions of labourers constantly unfit from malaria constitute an enormous economic loss to the country. These statements deserve the grave consideration of all statesmen who control and administer public health measures in India. An estimate, such as is being considered, will be based on experiences elsewhere.

Instances of successful localised anti-malarial campaigns.—Given a *limited* endemic malarial area and *unlimited* funds, any experienced malariologist can formulate a scheme for the reduction, and, in many places, the eradication of malaria in India.

(i) *Panama Canal Zone.*—Let us take the Panama Canal Zone and inquire whether what has been done there is reasonably possible in any single endemic malaria district of, say, 50,000 square miles in area in India.

In the Panama Canal Zone, when the canal was being constructed, the anti-mosquito work of the Sanitary Department was of the greatest significance and was carried on throughout the whole zone area. The real canal zone is about 50 miles long and 10 broad. It includes, as far as sanitation is concerned, the cities of Panama and Colon. The zone population is about 100,000, which includes 33,000 in Panama, 14,000 in Colon, and 52,000 in the zone itself. In the zone there are a number of small towns and villages, with several native towns and camps for the executive and labouring staff between them, all of which lie along the line of the Panama railroad.

The Sanitary Department had, apart from its office force, thirty sanitary inspectors, and employed between 1,200 and 1,300 labourers. Without entering into details it may be stated that all the known resources of the anti-malarial sanitarian were employed, backed by those of the United States Government, which looked upon expenditure as, at least in part, defensive. It is estimated that the sanitary works alone, excluding the upkeep of hospitals, cost about 15 lakhs of rupees a year. The construction of the Panama Canal was rendered possible by the anti-malarial measures adopted by the late Major-General Sir CHARLES GORGAS, U.S.A., and the powers which he had of enforcing them. This was previously an impossible task on account of the high mortality and sickness rate from malaria and yellow fever.

Malaria and mosquitoes then have been largely eradicated from the Panama Canal Zone, and were such measures, or some modification of them, *universally* brought into operation in India, a very considerable reduction of malaria, and an appreciable reduction of anophelines, would be effected. But the reduction of malaria in an area of, say, 500 square miles is a very different matter to that of such reduction in the whole of the Indian Empire, which extends over an area of 1,870,000 square miles, and has a population of about 300,000,000.

It is admitted that the conditions in the Panama Canal Zone are not parallel with

those in a country like India. The main anti-malarial efforts on the zone were to keep down anophelines by drainage and constant oiling, operations which are even *now going on. There are still plenty of anophelines in the area*; it seems impossible to get rid of them, and malaria still occurs in the zone villages, as it has done from time immemorial. What the authorities did was to *protect an imported labour force* by the above measures, plus mosquito-proof houses everywhere within the actual area of the canal works, and by quinine. It is understood that they are now economising and allowing native settlers in the zone for the first time, and it is all but certain that there will be a fair amount of malaria among them.

(ii) *Federated Malay States.*—The history of the reduction (in some parts, eradication) of malaria in the FEDERATED MALAY STATES during the last twenty-five years is one of the most thrilling records in the literature of tropical medicine. The anti-malarial work of that region has considerably expanded the vista of practical malaria control in all other malarial countries, and brought accuracy and precision to several of our measures. In the F.M.S. funds were strictly limited and were forthcoming only when the success of the work appeared to justify further expenditure. The remarkable success attained in towns, villages and plantations is most encouraging to all engaged in similar work in India, and especially to those engaged in that branch of anti-malarial work which aims at the reduction of malaria-carrying Anopheles. (See p. 329.)

(iii) Similar but more limited instances of the reduction of malaria have been brought about by anti-malarial measures in *Ismailia*, parts of *British West Africa*, *Algeria*, *Cairo*, *Port Said*, *Hong-Kong* and other places. In these instances practically all the known anti-malarial and anti-mosquito measures of modern times were employed.

Are such successes to be expected in India ?—The most optimistic and enthusiastic anti-malarial sanitarian could not devise any reasonable plan of campaign that would operate over an area of $1\frac{3}{4}$ million square miles in the satisfactory manner it did in the places referred to. In no circumstances is it conceivable that the same amount of concentrated energy and capital could be employed all over India. He might, however, reasonably hope to devise schemes that would considerably reduce malaria in the more endemic foci of India, and his schemes would in all probability be proportionally much less costly, as labour and material are cheaper. But in effecting this salutary change, even in comparatively small districts, he has before him an enormous undertaking.

The writer has been intimately connected with efforts that have been made to reduce malaria in India and Burma, especially in military cantonments, and with advising on anti-malarial problems, and knows from personal experience how much can be done to lessen the prevalence of malaria in our Indian Empire. The object aimed at in this book is to show how this may be achieved.

A.—PREVALENCE OF MALARIA IN INDIA

Malaria statistics in India.—Malaria, while varying in intensity from year to year (with meteorological and other conditions imperfectly understood), continues to be the great cause of sickness in India. The first task before us is that of gauging the dimensions of the evil to be contended with. Whilst there are few foci in India where malaria attains the same intensity as it does, say, in Tropical Africa and parts of Sicily, Macedonia, Thrace, etc., it may still be said that the actual figures contained in the *Annual Sanitary Reports of the Public Health Commissioner with the Government of India* show India to be the most malarious country in the world. These important statistics, greatly improved of latter years, are reliable for the Army. For the civil population they are not. In estimating the incidence of malaria among the latter, it is necessary to contrast the care bestowed on troops—in site, selection, and

construction of barracks, in feeding, in medical care and nursing when ill, and in preventive measures under continual control—with the contrary conditions obtaining in the civil population resident just outside cantonment boundaries. Moreover, these latter actually show a greater malarial incidence than the former. Accordingly, it must be concluded that malarial incidence and mortality is greater among civilians than in the Army. Now the statistics mentioned show that the average malarial incidence in the Army is about 20 per cent.; this rate would imply 60,000,000 cases annually in civil India. It is, however, likely that the poorly-housed and worse-fed rural Indians produce 80,000,000 cases yearly. Again, about 4,000,000 persons die annually in India from "fevers," in 80 per cent. of whom the cause is considered to be malaria. It is, on the whole, likely that at least a quarter of the sickness of India is of malarial origin, and that four-fifths of the malaria is rural, and it is improbable that more than a fifth of affected persons ever take quinine. The figures mentioned will now be considered.

Incidence of Malaria in the Army in India

Both directly and indirectly, in peace and war, malaria is the main cause of sickness in British and Indian troops.

(i) *British troops* : [1]

In 1921, a severe epidemic[2] year, 81 per cent. of hospital admissions were for malaria. Per thousand of strength the admissions and deaths were respectively 321·7 and 0·75 as against 175·4 and 0·43 in 1922 and 172·2 and 0·27 in 1923, which last was characterised by a very low malarial incidence throughout India, and an almost complete absence of epidemic malaria in the Punjab and North-West Frontier Province. In different Commands the admission and death rates per 1,000 varied in 1921 from 1088·3 and 2·89 to 63·1 and *nil* (in Burma).

Monthly Incidence of Admissions for Malaria in British Troops in 1922. *Total Strength* 60,166.

—	Admissions from Malaria in each month.												
	January.	February.	March.	April.	May	June.[3]	July [3]	August.	September.[3]	October.[3]	November.	December.	Total.
Northern Command	158	101	94	164	264	304	387	367	387	305	359	178	3,218
Western Command (excluding Waziristan Force)	98	59	58	105	120	155	181	156	201	163	67	44	1,407
Eastern Command	175	123	125	173	238	246	246	213	365	406	223	161	2,083
Southern Command	160	141	169	137	161	166	150	124	152	167	143	126	1,705
Burma District	3	3	2	—	7	16	18	8	6	9	13	35	110
Waziristan Force	47	21	24	33	73	123	119	154	146	205	153	60	1,158
Aden	6	14	10	9	14	40	9	5	1	4	1	6	125
Troops marching	3	—	—	3	—	3	—	13	5	7	12	1	47
Total admissions	650	462	478	624	877	1,112	1,110	1,040	1,252	1,356	971	611	10,552

[1] The malaria statistics of our European troops in India are the most reliable in that country, as the circumstances connected with all malarial infections are recorded on the men's *Malaria Case Sheets*, kept up in British Station Hospitals.

[2] For the definition of the term *epidemic* as applied to certain outbreaks of malaria in India see pp. 16 and 49 *et seq*.

[3] Note the peaks in June–July and September–October.

The corresponding Table for 1923 is almost the same.

The accompanying Table shows how malaria varies in different areas. This variation is fairly constant year by year. Clearly the disease is not under control.

Admissions and Deaths from Malaria in British Troops by Commands and Independent Districts in 1922.

Command.	Admissions.		Deaths.		Case mortality per cent.
	Actual	Ratio per mille.	Actual.	Ratio per mille.	
Northern	3,218	203·1	17	1·07	0·5
Western	1,107	237·1	2	0·34	0·1
Eastern	2,683	171·3	4	0 26	0 1
Southern	1,795	100 3	2	0·11	0·1
Burma district	119	63·4	—	—	—
Waziristan District	1,158	756·4	1	0 65	0·1
Aden Brigade	125	115·9	—	—	—
Troops marching	47	136·2	—	—	—
All India 1922	10,552	175·4	26	0·43	0 2
All India 1923	10,875	172·2	17	0·27	0·2

(ii) *Indian troops:*

Monthly Incidence of Admissions for Malaria in Indian Troops during 1922. Total Strength 147,840.

—	Admissions from Malaria in each month.												
	January.	February.	March.	April.	May.	June.	July.	August.	September.[1]	October.[1]	November.[1]	December.	Total.
Northern Command	702	388	419	367	654	734	571	685	863	1,203	1,091	613	8,290
Waziristan District	382	133	121	103	674	707	786	914	926	940	819	677	7,300
Western Command	134	74	92	117	170	190	240	347	483	504	286	174	2,820
Eastern Command	103	112	120	143	176	257	275	310	442	583	429	232	3,251
Southern Command	172	125	145	93	92	132	106	153	213	230	230	122	1,822
Burma District	17	10	20	12	21	27	59	46	39	41	64	58	423
Total admissions	1,761	1,027	1,138	1,205	1,960	2,340	2,125	2,541	3,033	3,571	3,007	1,988	25,706

Admissions and Deaths by Commands and Independent Districts in 1922.

Command.	Admissions.		Deaths.		Case mortality per cent.
	Actual.	Ratio per 1,000.	Actual	Ratio per 1,000.	
Northern	8,290	146 4	17	0·30	0·21
Western	2,820	136·7	4	0·19	0·14
Eastern	3,251	141 7	2	0·09	0·06
Southern	1,822	91·0	7	0·35	0 38
Burma District	423	84·0	2	0·40	0·47
Waziristan Force	7,302	388·0	53	2·82	0 73
Aden and Bushire	1,693	525·0	1	0·31	0·06
Troops on the line of march	104	176·3	—	—	—
All India 1922	25,705	173·9	86	0·58	0·33
All India 1923	22,046	158 1	99	0·69	0·44

[1] The main peak is in September–November.

There was a fall of 15·8 per 1,000 in the admission ratio of 1923 as compared with 1922. The average strength in 1923 was 143,234.

In 1921 the admissions and deaths per thousand of strength were 223·7 and 0·60, as compared with 173·9 and 0·58 in 1922, and 158·1 and 0·69 in 1923.

Prevalence of malarial fevers on field service.—Malaria, as statistical tables show, has markedly predominated in causing illness and inefficiency in both European and Indian troops in all Indian campaigns, unless these have been limited to the non-malarious season. Even then malaria relapses form a high percentage of the total admissions for sickness. See statistics for Waziristan Force in Tables on pp. 10 and 11.

The following Table from the *Annual Report of the Public Health Commissioner with the Government of India* for 1923, shows the incidence of malaria for that year in controlled bodies of men:

European Army of India												Indian Army						Constantly sick	Jail Population of India, 120,019.	
[illegible] Troops, 2,788.			Men, 63,139.				Women, 3,702.		Children, 7,915.		British Officers attached to Indian Troops, 2,218.			Men present, 143,234				
Admissions	Deaths	Invalids	Admissions	Constantly sick	Deaths	Invalids	Admissions	Deaths	Admissions	Deaths	Admissions	Deaths	Invalids	Admissions	Deaths	Invalids		Admissions	Deaths
298	—	3	10,875	291 89	17	29	200	1	15	2	330	—	1	22,646	90	302	722·00	26,000	131

Malaria in the Civil Population.—The comprehensive Table on the next page gives the number of cases of malaria treated in the civil hospitals and dispensaries in India in 1921, 1922 and 1923

This Table shows that approximately 8,000,000 cases of malaria, or 3 per cent. of the population, are annually treated in civil hospitals and dispensaries. Dr. C. A. Bentley, Director of Public Health, Bengal, estimates that in his province alone there are 28,300,000 cases of malaria requiring treatment annually. On a similar estimate worked out for the whole of India the number of cases of malaria calling for treatment is roughly 100,000,000.

Relative frequency in India of the three types of malaria.—The relative frequency of the three forms of malaria varies somewhat in different parts of India. In general terms benign tertian is by far the most frequent form; malignant tertian comes next; and, except in a few limited districts, quartan is the *least frequent*. There are regions in which quartan predominates, as in the Duars and the Andaman Islands, others in which malignant tertian is as prevalent as *benign tertian* fever in the latter half of the malarial season, as in the North-Western *Provinces*. The valleys of all the great rivers of India, the Indus, Sutlej, Ganges, Brahmaputra, etc., are heavily infested with malaria, chiefly the benign tertian form.

Relative frequency of the various malaria parasites, shown by microscopical examination of blood.—Among *British troops* in the year 1922 there were 10,552 cases of malaria admitted to hospital of which 10,514 cases were classified into probable new infections or relapses, and in 78 per cent.

—		State, Public, Local Fund and Private aided Dispensaries		State, Special and Railway Dispensaries.		Private non-aided Dispensaries.	Total	
		Indoor	Outdoor	Indoor.	Outdoor			
Bengal	1921	8,794	1,831,453	10,053	140,785	396,518	2,387,603	1921
	1922	7,391	1,545,878	8,116	129,786	339,748	2,030,919	1922
	1923	6,657	1,595,849	8,230	140,627	384,571	2,135,934	1923
Punjab	1921	5,014	653,554	3,096	135,197	8,217	805,078	1921
	1922	5,313	640,327	2,837	146,087	15,031	810,195	1922
	1923	7,209	953,003	3,340	214,402	17,826	1,196,677	1923
Madras	1921	7,927	453,005	1,010	32,372	36,516	530,830	1921
	1922	7,610	460,163	1,218	34,837	37,816	541,644	1922
	1923	8,369	528,406	935	36,825	36,724	611,277	1923
Assam	1921	2,301	232,664	2,573	23,602	7,640	268,780	1921
	1922	2,887	319,759	3,807	28,108	9,876	364,437	1922
	1923	2,422	293,145	2,381	26,558	9,140	333,646	1923
Bihar and Orissa	1921	4,116	611,890	2,544	76,171	129,531	824,252	1921
	1922	3,633	652,010	2,103	79,092	128,878	865,716	1922
	1923	3,624	719,302	2,553	80,577	126,452	932,508	1923
Central Provinces	1921	2,987	312,727	1,562	62,525	42,016	421,817	1921
	1922	2,610	272,885	1,429	55,799	34,525	367,248	1922
	1923	2,324	239,079	1,101	49,158	34,578	326,630	1923
United Provinces	1921	7,332	1,234,836	9,877	118,144	80,183	1,450,372	1921
	1922	6,265	1,058,180	7,319	100,055	84,887	1,256,706	1922
	1923	5,540	845,792	5,629	88,445	68,554	1,013,966	1923
Bombay	1921	9,768	451,240	5,546	89,467	247,778	803,799	1921
	1922	7,980	461,826	5,505	90,397	260,576	826,284	1922
	1923	7,158	434,088	5,141	81,746	231,449	759,582	1923
North-West Frontier Province	1921	1,557	192,561	5,554	35,861	4,980	240,513	1921
	1922	1,774	205,359	5,800	47,567	6,591	267,091	1922
	1923	1,645	187,472	5,403	53,105	7,872	255,587	1923
Burma	1921	12,761	256,776	7,819	31,842	*Nil*	309,228	1921
	1922	12,460	247,200	6,795	30,485	*Nil*	297,000	1922
	1923	13,468	239,823	6,709	31,414	*Nil*	291,414	1923
Total	1921	62,557	6,230,706	49,664	745,960	953,379	8,042,272	1921
	1922	57,923	5,863,647	44,929	742,813	917,928	7,627,240	1922
	1923	58,422	6,036,859	41,530	803,247	917,163	7,857,221	1923[1]

parasites were microscopically detected and classified. The results are shown below:

New infections: 4,054 = 38·42 per cent. of total admissions for malaria.

	Number of Cases	Percentage.
Benign tertian	2,553	62·97
Malignant tertian	682	16·80
Quartan	2	0·05
Mixed benign and malignant tertian infections	6	0·15
Diagnosed clinically	811	20·00
	4,054	

[1] For malaria statistics in civil population for 1924 see Appendix I.

Relapses : 6,460 = 61·22 *per cent. of total admissions for malaria.*

	Number of Cases.	Percentage.
Benign tertian	3,936	60·93
Malignant tertian	970	15·02
Quartan	7	0·11
Mixed benign and malignant tertian infections .	21	0·33
Diagnosed clinically	1,518	23·50
Malarial cachexia	8	0·12
	6,460	

Of the 10,875 admissions for malaria in 1923, 4,910 were classed as *fresh infections*, and 5,965 as *relapses of old infections*; and 84 per cent. of the cases were diagnosed by microscopic examination of blood films.

The following is a corresponding Table for the 25,116 cases admitted for malaria among *Indian troops* during the year 1922 :

Fresh infections : 5,507 = 21·42 *per cent. of total admissions for malaria.*

	Number of Cases.	Percentage.
Benign tertian	2,191	39·79
Malignant tertian	1,211	21·99
Quartan	21	0·38
Mixed benign and malignant tertian infections	22	0·40
Diagnosed clinically	2,030	36·86
Malarial cachexia	32	0·58
Total . .	5,507	

Relapses : 19,609 = 76·28 *per cent. of total admissions for malaria.*

	Number of Cases.	Percentage.
Benign tertian	6,223	31·73
Malignant tertian	2,199	11·21
Quartan	18	0·09
Mixed benign and malignant tertian infections	4	0·02
Diagnosed clinically	11,076	56·48
Malarial cachexia	89	0·45
Total . .	19,609	

Among Indian troops *the admissions for relapses of old infections formed* 76·28 *per cent. of the total admissions for malaria in the year* 1922.

In 1923 the total admissions for malaria were 22,646; of these, 5,042, or 22·27 per cent., were fresh infections, and 17,604, or 77·73 per cent., were relapses of old infections. For corresponding tables for 1924 see Appendix I.

These groups of Tables show that among British troops there are 3·7 benign tertian *fresh cases* to 1 of malignant tertian, and of *relapse* cases, 4 of benign tertian to 1 of malignant tertian. Among *Indian troops* the corresponding ratios are 1·8 to 1 and 2·8 to 1.

The small percentage of the cases which were diagnosed as fresh infections is notable in both Tables. If, in Indian troops who have received quinine treatment and careful medical attention, relapses form 76·28 per cent. of all cases, there would be but little exaggeration in concluding that the great majority of infections in rural India occurring in any one year will relapse in the next.

As indicating the vast diagnostic improvement which has occurred in India of recent years, it may be noted incidentally that with 36,257 admissions for malaria in the Army during 1922 there were only 77 returns of "pyrexia of uncertain origin."

B.—MORTALITY FROM MALARIA IN INDIA

Malaria is usually a benign and protracted disease, but it is liable to various complications, and to be associated with intercurrent maladies, such as pneumonia, dysentery, anæmia, infantile diarrhœa, etc., which may end fatally. The great majority of the malarial deaths occur among the children of the masses in rural areas, only a comparatively small proportion of whom are treated by trained medical men; therefore the cause of death is seldom confirmed. The headman of the village is the local registrar of deaths; he, in the absence of plague, cholera, smallpox and other epidemic disease, enters all deaths as due to "fever." With children it is usually the intensity of the parasitic invasion that kills, a true malarial toxæmia resulting, and most of the deaths are correctly recorded as due to "fever," the nearest approach to accuracy we can at present expect. If malaria cause death in adults it usually does so indirectly.

Mortality from malaria in the civil population in India.—Year after year the *Annual Report of the Public Health Commissioner with the Government of India* emphasises the great difficulty of carrying out a detailed analysis of the deaths ascribed to "fevers." In most provinces the seasonal fluctuations in the number of fever deaths indicate that malaria plays an important part in the production of the total mortality. In 1921 there were 4,761,287 deaths from fevers, in 1922, 3,689,086, and in 1923, 3,706,298.

"Fever statistics do not represent malaria, but careful verification of selected areas has led to correction factors being evolved which allow of epidemiologists reading into such figures as are recorded much that at first sight would appear to be impossible or unjustifiable. Thus, broadly speaking, and subject to variation in different areas, we may take it that one-third at least of recorded 'fever' deaths are due to true malaria."[1]

For the first time the *Annual Report* for 1923 publishes an attempt to classify the diseases making up this fever group, and shows their distribution in the various provinces. The results as regards deaths from malaria are given in the following Table.

		Total deaths from Malaria.	Death-rate per 1,000 from Malaria.
Bengal	R	532,325	12·2
	T	7,574	2·4
Assam	T	242	
United Provinces	R	643,110	15·18
	T	22,200	7·30
Bombay	R	31,735	2·06
	T	3,222	0·80
Burma	T	2,258	1

R—rural areas. T—towns.

It is recognised that these figures are inaccurate, but "it is the beginning of an attempt to get more reliable data."[2] (See Appendix I.)

In districts with hyperendemicity or high endemicity, as contrasted with

[1] *Annual Report of the Public Health Commissioner with the Government of India* for the year 1923, Part I, pp. 107, 108.

[2] *Ibid.*, p. 107.

healthy districts, there is an increase in the total death rate; there is also a much greater mortality among infants and very young children. On this account a considerable amount of immigration takes place from the former to the latter, which is specially seen in Bengal and the Punjab. Even in ordinary endemic malarious areas the average duration of life is shorter, and the infant mortality higher, than in healthy areas. In hyperendemic and severely endemic malarious districts the tendency is, on the whole, for the population to decline, whereas in healthy districts, *caeteris paribus*, there is a moderately rapid rise in the population.

C.—GEOGRAPHICAL DISTRIBUTION OF MALARIA IN INDIA

The relative prevalence of malaria in India is indicated by the following terms which signify definite *average spleen rates* among children; they are employed in the Malaria Map of India and, usually, in official and other records on malaria:

Healthy area.—Rate not over 10 per cent.

Moderately endemic area—Rate between 10 and 25 per cent.

Highly endemic area.—Rate between 25 and 50 per cent.

Hyperendemic area.—Rate is above 50 per cent.

Malarial foci are *endemic* when conditions favourable for transmission are present year after year; *potential* where they may be realised at any time, although one or other factor is for the time being absent: *epidemic* when some new condition has facilitated transmission in an endemic, or made it possible in a potential, focus. Malaria is never pandemic in India in the same sense that influenza may be.

The Malaria Map of India, specially prepared for this book by Lt.-Col. S. R. Christophers, C.I.E., O.B E., F.R.S., I.M.S., Director, Central Malaria Bureau, Kasauli, is the first of its kind constructed. Because of the defects in the statistics of malarial incidence, and the fact that many parts of the country still remain unsurveyed, the map is incomplete, but it portrays the varying degrees of prevalence of malaria in the geographical divisions of India, as perfectly as available figures permit. (See Appendix II.)

Incidence of Malaria in Provinces *and* Districts.—For our purpose here we may divide India into three main regions—*Himalayan India, Middle India* and the *Deccan.*

Himalayan India, generally over 1,000 feet in height. It includes:

1. Himalaya East and Sikkim (east of Nepal).
2. Himalaya West and Kashmir (west of Nepal).

At the foot-hills of both these areas there are elongated tracts of hyperendemic malaria.

3. The North-West Frontier Province, which contains the notoriously malarious valleys of the Indus and its tributaries and much irrigated land. The Indus and its branches are subject to serious flooding with inundations, which are periodically associated with widespread epidemics of malaria.
4. Baluchistan, a thinly populated, arid mountainous district with, generally speaking, mild malaria, but small patches of severe, endemic infection.

Middle India, the plains of Northern India, a widespread alluvial tract under 1,000 feet above sea level, includes:

1. Sind, which forms the delta of the Indus, a rice-growing area, with, usually, moderately severe malaria, but liable to periodical epidemic outbursts.
2. Rajputana West with the Bikanir Desert, a thinly populated, millet-growing country with moderate endemic malaria.
3. South-Western Punjab, a semi-desert area, with a scanty population and moderate endemic, but without epidemic, malaria.
4. East and North Punjab, a heavily populated wheat-growing area with, usually, moderately severe endemicity, but subject to overwhelming and appalling outbursts of epidemic malaria—*it is the home of this latter form of the disease* (see pp 49–51, Appendix II).

(especially in the western half and north), and divided into elongated sections by rivers and hills running north and south. It may be divided into Upper, Middle and Lower Burma. In the Northern region the malaria varies from severe endemicity to hyper-endemicity; blackwater fever is not uncommon; in the Middle region there is ordinary endemic malaria, which in some years becomes severe. In Lower Burma the malaria is typically endemic. The lower slopes and foot of the Northern and Southern Shan Hills and Chin Hills are afflicted with intensely severe malaria, and blackwater fever is met with, especially in the latter hills. Epidemic malaria does not occur in Burma.

The geographical distribution of Epidemic Malaria is specially dealt with on pp. 19–51 and Appendix II.

It is interesting to note that there are many districts in the plains of India which, as regards malaria, are in the healthy group, and there are some districts, such as the small Jaisalmer State, in which there is almost entire absence of malaria.

Malaria flourishes in all its endemic centres in India with unfailing regularity, summer and autumn with greater or less severity. Sometimes, however, it goes beyond the bounds of its normal limits and assumes the character of an epidemic, spreading to places not ordinarily attacked. The intensity of malaria undergoes changes even in its endemic centres, sometimes almost disappearing for a time, at others showing a tendency to high endemicity. Some districts of the Punjab and the North-Western and Western Districts of the United Provinces are periodically invaded by epidemics of malaria of terrible severity (p. 49 *et seq.*).

Malarial fevers are usually most severe and persistent in low-lying coast districts; deltas of large rivers in India are especially liable to outbursts of epidemic malaria. This is true of all bodies of water situated in low-lying places. These are the localities in which we get (1) a dense population, (2) a large floating population many of whom are susceptible to malaria, and (3) swarms of malaria-bearing anophelines. Hence we find malarial fevers in India very prevalent in the low lands in the neighbourhood of the large rivers such as the Ganges, Indus, Godaveri, Mahanadi, Kistna, in Assam along the Brahmaputra, in which province it is also very virulent on the lower slopes of the hills and in the valleys along the branches of the Brahmaputra; in Burma it is specially malignant along the valleys of the Irrawaddy, Chindwin and Moo—some of the worst malignant infections the writer has seen were in our troops returning from expeditions along the upper reaches of these rivers in the war of 1885–87; in Manipur (about 3,000 feet)—which is a small territory 30 miles long by 10 wide, surrounded by low hills and intersected in every direction by streamlets and irrigation canals, every available square yard taken up with rice-fields—malaria is exceedingly prevalent. Along these rivers there are unlimited breeding grounds for anophelines.

Well-drained uplands and carefully cultivated districts in India are generally healthy. But dry elevated land and even sandy tracts may be very *malarious*.

Not only does the degree of prevalence of malaria vary to the extent just indicated in different districts, towns, garrisons and communities; it will in the main be found to vary in the same locality from season to season. The causes of these variations are not always obvious. Acquaintance with the various links of the chain forming the life-cycle of malaria parasites is indispensable for their elucidation. Some of the conditions operate indirectly and may affect different parts of the cycle in quite opposite ways. Local variation in malarial prevalence in endemic areas is affected by the number of anophelines implicated in carrying local malaria, the economic and hygienic conditions of the inhabitants, the degree of immunity acquired by the community, the

5. Western Division of the United Provinces, a heavily populated wheat and rice-growing area, normally with ordinary endemic, but liable to occasional epidemic malaria where it is co-terminous with the Punjab, and, so it would seem, an extension from the latter.

6. United Provinces, East, a heavily populated rice-growing country with typical endemic malaria, but with patches of hyperendemicity, where it runs into the foot-hills of the Himalayas; it is not subject to epidemic malaria.

7. Bihar, a country in which rice forms 60 per cent. of the crops, with a population of moderate density. Is also a typical endemic malarial area.

8. Deltaic Bengal, densely populated by the Bengali race; rice forms 80 per cent. of the crops; normally afflicted with ordinary endemic malaria, but is liable to hyperendemic outbursts. It is on the whole healthier than Upper Bengal.

9. Eastern Bengal, moderately heavily populated; 80 per cent. of the crops consist of rice, it is subject to annual flooding over extensive tracts. Normally it is afflicted with severe endemic malaria, but, like the Deltaic region, this in some years becomes hyperendemic or even epidemic.

10. Assam, the Brahmaputra valley, a densely populated rice-growing country, that suffers from severe endemic malaria, with patches of hyperendemicity.

11. Gujarat, in the extreme west of the Northern Plains region, a thickly populated area with, usually, moderate endemic malaria, but subject to outbursts of hyperendemicity; epidemic malaria occasionally occurs.

THE DECCAN.—An extensive plateau of basalt and gneisses (especially granitoid), generally over 1,000 feet high, here and there densely populated, growing mixed crops, with moderately endemic malaria, interspersed with patches, small and large, of severe malaria. It includes the Eastern Plain, Central Indian Plateau, East Satpuras (Plateau), Deccan (Plateau), South India, the Chota Nagpur Plateau, Jeypore Hill Tract and the River Valley Plains, including Orissa.

1. Eastern Plain.—Under 1,000 feet high. It includes the moderately well populated rice-growing districts of the Carnatic Plain, Tanjore, Coimbatore, etc., with mild endemic malaria; much of it is unsurveyed. Also the Madras Hills (Nilgiris, Palnis, etc.), with moderately severe malaria at the foot of the hills. Likewise Madras Coast North, part of the area south of the Godaveri, and the Godaveri, Kistna and Nellore districts, all rice-growing areas, with a moderately full population, and with, generally, ordinary endemic malaria. Madras Coast North, however, includes the Jeypore Hill Tract, a rice-growing district with severe endemic, and in some years even hyperendemic, malaria.

2. River Valley Plains, including Orissa. Well-populated area, containing much flat rice-growing land in the valley of the Mahanadi, with moderately severe endemic malaria.

3. Central Indian Plateau, which includes Eastern Rajputana and Central India West, which have mild malaria.

4. East Satpuras (Plateau), which embraces Central India East and Central Provinces West, a thinly populated wheat-growing area, with mild endemic malaria, except at the foot-hills, where it is severe.

5. The Deccan Plateau proper, which embraces the Hyderabad State, with the upper part of the Godaveri, and the Bombay Deccan, mostly with mild malaria interspersed with many really healthy districts.

6. South India, which includes the Madras Deccan (Cuddapah, Kurnool, etc.)—rice-growing areas, well populated, with mild endemic malaria—and Mysore, which is healthy.

7. Chota Nagpur Plateau, thinly peopled by aboriginal races, rice-growing, with mild endemic malaria.

8. River Valley Plains of the East Central Provinces; contains the valleys of the Godaveri and Mahanadi; well populated; much irrigated land under rice cultivation; ordinary endemic malaria with patches of greater severity.

9. On the West Coast we have Konkan in the Bombay Presidency, and Malabar in the Madras Presidency, both with heavy rainfalls, ordinary endemic malaria, with extensive areas of high endemicity, sometimes hyperendemicity.

BURMA.—A densely populated rice-growing country, with a heavy rainfall

highly probable that it is only in the warmer places that oocysts would survive the winter. MITZMAIN[1] records the examination of 1,211 hibernating anopheles in the Mississippi delta, prior to May 15, with the object of discovering any evidence of winter infection. He found no infection and concludes that in the area investigated man is the sole winter carrier.

It has been shown that with an average temperature of 25° C. (77° F.) the benign tertian parasite completes its development in *A. maculipennis* in eleven days, with a temperature between 15° C. (59° F.) and 23° C. (73·5° F.) in fifteen days (ROUBAUD). The lowest temperature at which it develops in *A. maculipennis* is between 15° C. (59° F.) and 17° C. (62·5° F.), and then the cycle is not completed for fifty-three days (JANCSO). At 25° C. (77° F.) the malignant tertian parasite develops more slowly than the benign tertian in the mosquito named.

Humidity.—This is a significant factor in connection with the occurrence of malaria. The typical malarious locality is low and marshy, or in the vicinity of rivers, lakes and large accumulations of water. Some regions in India, almost free from malaria in the hottest part of the dry season, become very malarious shortly after the commencement of the rains, and their malarial intensity becomes greater during the autumn. Moisture is essential for the development of the eggs and larvae of anophelines.

The great importance of humidity of the soil is shown by the association of malaria with marshes, *jheels*, swamps and the banks and drying beds of rivers and sea coast. The period following the overflowing of rivers and inundations of the surrounding country is specially malarious. This latter condition is imitated artificially over large tracts of India by the irrigation of rice and other cereal crops.

Observations on atmospheric humidity.—Laboratory experiments show that captive Anopheles live much longer in humid than in dry air. Lt.-Col. E. C. HODGSON, D.S.O., I.M.S., as the result of a series of special observations on the effects of humidity, is of opinion that in dry air the temperature of a mosquito's body approximates by evaporation to the wet bulb temperature, in nearly saturated air to that of the atmosphere. He has shown that exflagellation with fertilisation occurs only with the wet bulb between 18° and 22° C. and holds that anti-malarial prophylaxis is necessary only when these conditions are fulfilled. When the air is moist Anopheles seek the open. Dr. C. A. BENTLEY some years ago published[2] a table showing how atmospheric humidity affected the monthly findings of sporozoites in *A. stephensi* in Bombay; the infection rate was highest when the humidity was greatest, and lowest or altogether absent when the humidity was comparatively low.

Observations on atmospheric humidity and temperature.—Lt.-Col. C. A. GILL, I.M.S.,[3] refers to the relative influence of temperature and humidity on mosquitoes and on the transference of malaria, and reports experiments in which *Culex fatigans* and *Proteosoma grassii* were employed. At 27° C. (80·0° F.) *C. fatigans* cannot survive for more than five days if the relative humidity be below 48 per cent., a time not long enough for sporozoites to form. If this apply to Anopheles, they, too, would not live long enough for malarial sporozoites to develop. At the same temperature with a humidity of over 48 per cent, mosquitoes survive and growth of oocysts and sporozoites proceeds normally. In the high temperatures of the Punjab in April and May successful feeding does not take place if the mean relative humidity be less than 40 per cent. If it exceed 50 per cent. successful feeding is assured. Regarding temperature, the minimum at which *C. fatigans* will live is not known. It will not feed at 10° C. (50° F.); at 26° C. (78·8° F.) it feeds and egg development takes place rapidly when the mean humidity is relatively high, but not when it is relatively low. At 40° C. (104° F.) it dies in about fifteen minutes. Regarding temperature,

[1] *Is Mosquito or Man the Winter Carrier of Malaria Organisms?* U.S. Public Health Service, *Public Health Bulletin*, Dec., 1916, No. 84.
[2] *Paludism*, No. 3, 1912.
[3] *Tropical Diseases Bull.*, Vol. 18, No. 5, pp. 328, 329.

number of susceptible people present and other factors. Regarding the anophelines, the same physical conditions in different provinces and districts or even towns and cantonments may be associated with many or few of them; this may be found to be connected with the habits of the species of anophelines carrying malaria, with the presence or absence of the natural enemies of mosquitoes, etc.

Apart from recrudescences of endemic malaria, there are occasional temporary visitations of malaria to localities that are normally non-malarious. This might arise from a large influx of malaria-infected persons into a region where there are potential malaria-carriers, or from the infiltration of malaria-infected anophelines. The writer recalls an outbreak of malaria in 1900 and 1901 in the troops and police battalion at Kohima (Khassia and Jantia Hills, 6,500 ft.), when a double company of Gurkhas returned to Kohima saturated with malignant tertian malaria after temporarily garrisoning certain outposts at the foot-hills of Bhutan. *A. maculatus* and *A. minimus* are normal inhabitants of Kohima. The disease spread rapidly in the summer of 1900, and fresh infections, acquired locally, did not disappear until the end of 1901, anti-mosquito measures and vigorous quinine treatment being employed throughout that time. The same occurrence has been noted from time to time at other hill stations—Shillong (4,500 ft.), Kurseong (5,000 ft.) and even Murree (6,500 ft.).

D.—CONTRIBUTORY CAUSES OF MALARIA IN INDIA

While the direct cause of malaria in man is an infection of the red cells by species of protozoal organisms, which infection is transmitted through certain species of anophelines, there are many contributory endemiological and epidemiological factors which it is convenient to consider before dealing with the parasites of malaria and the relations of mosquitoes to malaria in man.

These *contributory factors* are—meteorological relations and telluric conditions favourable to malaria, the influences of marshes and other collections of water, and the relation of the anopheline population to malaria. These are factors which enter indirectly into the causes of malarial infections. They favour the development of the parasite in the body of man or mosquito, or indirectly assist in infection through mosquitoes.

I.—Meteorological Relations of Malaria

Temperature.—Temperature, as far as India is concerned, can only be looked upon as a predisposing cause affecting the breeding of anophelines, the development of malaria parasites in anophelines, and the multiplication of malaria parasites in the blood of man. One of the causes of the reduced malaria in very hot, dry years is the great reduction of Anopheles so brought about.

Observations on atmospheric temperature.—The following observations bear on this important matter.

Jancso has shown that the zygote ceases to develop in the mosquito at about 15·6° C. (60° F.). Above this temperature, to a certain limit, the development goes on more rapidly, and may be completed and sporozoites formed in as short a time as six or seven days. The effect of intermittent application of lowered temperature is only to delay, not to prevent development. A prolonged low temperature is stated to bring about degeneration of sporozoites in the salivary glands. Wenyon [1] has shown that in the Balkans hibernating infected mosquitoes carry the malaria parasite in the oocyst stage throughout the winter; he states, however, that it is

[1] *Malaria in Macedonia*, 1915–1919, pp. 65, 66; also *The Lancet*, July 3, 1920.

provide sufficient water for oviposition, and sufficient time for hatching. Overflow of large rivers in India has for ages been recognised as a prolific cause of epidemics of malaria, or, at least, hyperendemicity. The Indus, Sutlej, Jhelum, Beas, Jumna, Ganges, Godaveri, Kistna, Brahmaputra and other Indian rivers periodically overflow their banks, and malaria appears in the tracts affected shortly after the subsidence of the overflow. This leads us to infer what actually is the case—that mosquitoes flourish in the shallow pools and puddles left after this subsidence, and do not thrive in great collections of rapidly flowing water, where they are washed away in the torrents and eaten by fish. When the pools left are flooded, washed out and converted into deeper collections of water, the evolution of mosquitoes from ovum to imago is greatly interfered with. During a dry period following rapidly upon heavy rains or freshets, malaria outbreaks are severe and frequent. This phenomenon is constant and pronounced all over India. In the same way improper irrigation, by pool production, increases malaria.

The association of rainfall with malaria is more or less constant; Lt.-Col. C. A. Gill has shown this to be so regular in the Punjab that from the precipitation in July and August the autumn incidence of malaria has been forecasted with a considerable degree of general accuracy. On the other hand, drought has disseminated and intensified malaria by driving malaria-infected famine-stricken people into less malarious parts.

While wet years in Northern India, and especially in the Punjab, considerably increase the incidence of malaria, there are many stations in which, even in dry years, these fevers are very prevalent, such as Peshawar, Kohat, Mardan, Lahore, Amritsar, and the irrigated areas of the Punjab generally, the explanation being that the anopheline population is maintained by the large number of irrigation channels in use. In irrigated areas with a low rainfall, such as the United Provinces and Oudh, the top of the malaria curve coincides with the melting of the snows in the hot weather, with the corresponding rise in the rivers and increase of irrigation. In certain other areas the early torrential rains flood the country for a time and cause a lowering of the malaria curve while the flood lasts.

In general terms it may be stated that malarial fevers are most prevalent in India during the years of the heaviest monsoon rains—these are the years in which we get outbursts of high endemicity—and this is particularly the case in the level plains, and localities in which the drainage is slow or in any way obstructed. Conversely, it is a well-recognised sequence that in comparatively dry years, with a shortage in the rainfall, the amount of malaria is much below the average, the dry years being on the whole the healthiest, though not usually the most prosperous.

Winds.—Malaria we now know is not due to *miasmata* carried by the wind. The only effect of wind on malaria is that of fostering or preventing the flight of Anopheles on the one hand, and predisposing man to chills on the other. Normally the diffusion of Anopheles by wind operates only over limited distances; hills, trees and other obstacles may protect houses to leeward of breeding-places of anophelines. This is explained by the known habits of anophelines, which are weak and low fliers, rise only a few feet above the ground, and in winds seek shelter in trees, brushwood and bushes, and even in grass; they are easily hindered in their flight by obstacles, and are destroyed by storms. It must be stated, however, that reliable observations as to the effects of winds and storms on mosquitoes are meagre, if not actually non-existent. Good electric fans and *punkahs* creating strong currents of air force Anopheles to seek shelter away from them.

however, the details which apply to Culex and Proteosoma are not quite evidential of what happens in the case of malarial plasmodia and Anopheles. For example, *A. culicifacies*, *A. stephensi* and *A. pulcherrimus* at 40° C. remain full of life. Lt.-Col. GILL's illuminating essay[1] should be read *in extenso*. It is highly probable that in India the humidity factor is more important in influencing the spread of malaria than the temperature factor.

Although more investigation is necessary, two dominant facts appear to stand out. When the atmospheric temperature falls below 16° C. (60·8° F.) the parasites of malaria cease to undergo further development in the midgut of infected anophelines. High atmospheric humidity is favourable to the development of malaria parasites in infected anophelines

The bearing of such observations on field conditions.—In temperate climates malaria is active only during the warm season. In India and in the tropics generally it prevails in the wet season While a high temperature may favour the development of malaria parasites in anophelines, concomitant atmospheric dryness may kill the mosquito.

In endemic malarious areas anophelines of certain species winter in houses, huts and stables, and the malaria parasites in a large number of them perish. In the spring, in many parts of India, the mosquitoes become re-infected from cases of relapses. It is through these relapses or residual cases that malaria is maintained from one year to another.

In malaria field work in rural districts the effects of high humidity are very obvious in the morning and evening; a heavy haze and mist overlie the fields. This may explain the use of the terms "miasma" and "telluric influence" in bygone times.

In parts of India there is a definite seasonal and geographical distribution of malignant tertian fever, attributed by some authorities to the fact that this parasite, in the mosquito, requires a higher air temperature than does either the quartan or the simple tertian parasite. This may be so, but it is not the full explanation, for both *A. culicifacies* and *A. stephensi* can successfully be infected from selected crescent patients at an atmospheric temperature of 33·3° C. (92° F.), and also at 40° C. (104° F.). A more elaborate theory has recently been advanced (see pp. 24, 25). Great falls of temperature in malarious places are important in respect of their being associated with relapses from chills, the latter operating by lowering the physiological resistance and thus permitting latent malaria parasites to multiply.

Rainfall.—The total annual rainfall of India has a very definite distribution. The chief characteristics are: (1) *An area of deficiency* in North-West India, which may be mapped out by following the limit of annual fall under 20 inches; (2) *three areas of very heavy rainfall*, of 75 inches or over; one over Eastern Bengal and Assam, another consisting of a narrow strip along the West Coast of the Indian Peninsula, and a third in Burma, along the West Coast and for some distance inland; (3) *an area of more moderate rainfall* over Bengal and the North-East of the Deccan (50 to 75 inches), extending over much of the United Provinces (40 to 50 inches); and (4) a broad belt extending from north to south, in which the rainfall is between 20 and 40 inches.

The amount of rainfall, and the period over which the rainy season continues, have an important influence on the prevalence and distribution of malaria in India. Rainfall conduces to the production of malaria because it is favourable to the development of larvæ of anophelines. Heavy torrential rains have the effect of washing away mosquito larvæ, whilst intervals of dry weather dry up the pools and may be associated with desiccation of larvæ. It is probable, however, that such torrential rains largely wash away the comparatively small fish that consume larvæ. The most favourable conditions for mosquitoes are intermittent and moderate rainfall with intervals of sunshine, since these

[1] *Ind. Jl. Med. Res.*, April, 1921; *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XIV, January, 1921, p. 77.

grounds for malaria-bearing anophelines and cases of malarial infection are always present. Further observation from, say, the middle of March to the middle of May should elicit whether this is actually so, and whether the malaria-carrying species of anophelines disseminate malaria at that particular season. This could be ascertained by taking a sufficient number of anophelines in native huts at that time and determining the sporozoite rate."[1] Several observers have since investigated this subject and verified the statement.

It is most important that we should know the beginning and end of the season during which anophelines breed. There are some stations in which the winged malaria-carrier cannot be found after October 15, others in which it may be found at the end of October and well into November, and in a large number of stations in the Deccan and along the East and West Coasts of Southern India it may be found all the year round. In all stations in Northern India a certain number of anophelines continue on the wing and carry malarial infection for weeks, or even months, after the breeding season is over.

There may then be two malarial seasons in parts of India, a short one during late spring or early summer and the usual long one during and after the south-west monsoon. Four possible causes for the spring season require consideration:

(a) Hibernating mosquitoes, infected in the previous autumn, resume feeding in the first warm days of spring, and thereby inject matured sporozoites.

(b) Hibernating uninfected mosquitoes, revivified by the warmth, become infected from latent or relapsing malarias, particularly from children who are so extensively infected in endemic areas.

(c) Hibernating mosquitoes, revivified by the warmth, oviposit in the collections of water produced by the spring rains above-mentioned, and the new brood becomes infected from latent and relapsing infections.

(d) The spring outbreak of malaria is the first obvious manifestation of a human autumnal infection.

Much further investigation is required before these causes are elucidated, but it may be noted that most authorities appear to consider that survival over the winter of malaria parasites in mosquitoes must be rare. Some observations[2] by the writer lead him to the conclusion, from which subsequent events have necessitated no withdrawal, that the third explanation holds. Anterior to the spring showers there were few Anopheles on the wing, and sporozoites were not found in those species which were local vectors, whereas in the young brood, appearing four to five weeks later, sporozoites were present in a small percentage. The possibility of a long latency of autumnal infection is being more widely supported at the present time than hitherto.

The following interesting speculation has recently been advanced. It is deserving of close attention and further investigation. To some extent it fits in with the writer's experience. It correlates seasonal incidence of malaria with seasonal consumption of quinine. Owing to quinine having a less specific effect on the benign tertian parasite than on the malignant tertian, and because of the general cessation of quinine ingestion during the winter, the year in India starts with many more active carriers of *Plasmodium vivax* than *P. falciparum*. Mosquitoes become correspondingly infected. As symptoms appear and quinine is again ingested the gametocytes of benign tertian are rendered impotent, while those of *P. falciparum* are not. Then, too, the latter tend in heavy infections to be more numerous than

[1] *Report on a Malaria Survey of the 7th (Meerut) Division*, November, 1909, App. II.
[2] *Ibid.*

Climatic and seasonal relations of malaria.—The climate and season of the year are important factors both in the incidence of malaria and development of anophelines. Malaria is prevalent when the conditions of heat and moisture are favourable to the development and activity of anophelines and plasmodia. While in temperate climates malarial fevers occur only during the warmest season of the year, in the tropics they prevail for much longer periods, their incidence being highest during the rainy season and the period following it. Most cases occurring during the first half of the year are considered to be relapses and not cases of initial infection.

Season has a marked influence as regards the number of cases met with in any locality, so much so that in India one particular part of the year is called the *malarial season*. This usually occupies about four months, and these months are different in different localities. They are generally August to November, but they may be much earlier, as in Burma. When epidemics happen, warnings of their advent are given by the rise of malaria in August and September, but the real epidemic time (when they attain their maximum intensity) is in October and November. This incidence is to a large extent affected by the prevalence or fewness of anophelines, although this is not the entire explanation, especially in localities where there are few malaria-bearing anophelines with severe malaria in man.

There are in endemic centres periods of maximum and minimum incidence—the maximum is usually the autumn, and the minimum the spring and early summer months. The maximum prevalence is therefore towards the end of, and shortly after, the rainy season.

Spring rise of malarial incidence in India.—In many parts of India heavy falls of rain in March, April or May are connected with a sharp, short rise of malaria a month or six weeks later, which some hold as due to relapses arising from chills caused by reduced atmospheric temperature. Were this so, the increased incidence would occur immediately or shortly after these falls. It is more probably due to malaria-bearing anophelines taking advantage of the presence of water to oviposit, these additional malaria cases being due to infection through the new generation of anophelines. Observations made at these rainfall periods in late spring and early summer would decide this matter. This rise in the curve of malarial incidence attains its maximum at different times. In the United Provinces, Central Provinces and Punjab it is at its highest in May; it is earlier in Madras, Assam and Burma. It may be a few weeks earlier or later, and in some years the rise may be quite high and prolonged. The writer made this observation in 1909. Hibernating malaria-infected anophelines come forth at this time and infect man for a short season.

Accepting the fact that anophelines are the only carriers of malaria from man to man, malarial fevers must necessarily, apart from relapses, be seasonal in most places in India, the maximum period of incidence of these fevers closely corresponding with the time when the anophelines implicated are most numerous. In some stations of the United Provinces, Central Provinces, Madras Presidency and Burma infection through anophelines occurs for one or two months during the late spring and early summer, if during March, April or May there happen to be heavy falls of rain. This means that in this circumstance there may be two malarial seasons in such places, one which is short in the late spring, the other the usual summer-autumn one. "It is possible that in stations where there are perennial breeding grounds, the occurrence of a heavy shower of rain during the period named is not necessary to bring about these infections. The subject is of considerable importance in the endemiology of malaria, and should not be difficult to prove or disprove where potential breeding

Indus, Nerbudda, Kistna, etc.) are made up of soils of this description, and some of the most important towns and stations of India are placed on such sites. The deltas of great rivers present these alluvial characters in the highest degree, and should never be chosen as building sites. If they must be used only the most thorough, deep drainage can make them healthy. Impervious soils impenetrable to water, and which permit of the formation of pools and collections of stagnant water, are the most dangerous. Marshes and swamps, where the surface of the soil is partially covered with water, are very favourable to anophelines. Adequate and scientific drainage and the formation of canals in such areas are followed not only by reduction of malaria, but by improvement of the general health. Vegetation, *per se*, has nothing to do with malaria—malaria may abound in its most concentrated and deadly form where little or no vegetation exists, and it may be absent in the densest jungles and other places where vegetation is luxuriant. The most putrid animal decomposition with an abundant evolution of ammonia and sulphuretted hydrogen is not associated with the production of malaria. Decaying vegetable and animal matter assist breeding by yielding food to mosquitoes.

The one essential and constant relation of soil to malaria is the presence of facilities in the soil for the collection of surface water wherein mosquitoes can breed. Hence we find that low-lying lands covered with rank vegetation and marshes, such as river estuaries, are frequently endemic malarial localities. In such cases the complete drainage of the soil, or the flooding of the surface, at least partially, and sometimes entirely, renders them non-malarial. It was formerly thought that malaria was produced by excavating or upturning the soil in endemic malarial areas—that malaria was due to a poison or miasm which was contained in certain soils, and that when such soils are dug up or turned, the poison made its exit. This is the basis of what was known as the *telluric origin of malaria*. The records of the history of malaria contain many instances of malaria said to have arisen in this way. We now know that in a large number of these instances the cases were either not malaria at all, or were merely relapses of malarial fever occurring in those employed in such work—cases in persons who had previously suffered from malarial fever—whilst others were probably cases of initial malarial infection acquired in the usual way by the bites of infected anophelines at some antecedent date. It is probable that some of the outbreaks of malaria formerly attributed to turning up of the soil or the clearing of jungle were, at least partly, due to these operations rendering available breeding-places of a type suitable for particular species of anopheline malaria-carriers. That this was the case as regards *A. maculatus* in the Federated Malay States has been fully demonstrated (p. 329). These explanations partly account for the large number of labourers infected in road-making, in making railway embankments, excavating canals, in all of which occupations thousands of persons are housed together in temporary thatched huts adjacent to the works, surrounded by marshes or by collections of water contained in borrow-pits which they have made during the course of the work—in which excavations myriads of anophelines breed. This, however, is not the complete story. It is a sound rule that works connected with disturbance of the soil should, whenever practicable, be carried out during the non-breeding season of anophelines.

Subsoil water-level in relation to malaria.—The relationship of malarial diseases to the level of the subsoil water, and to meteorological and climatic conditions, was forcibly brought to notice by LANCISI (1718), who also attempted to prove experimentally the connexion of malaria with marshes.

the former. Consequently mosquitoes steadily become more highly infected with malignant tertian malaria and transmit it in an increasing degree, so that by autumn it is the prevalent infection in many parts of the country.[1] There are, however, large areas in India in which this seasonal variation does not occur, benign tertian malaria predominating throughout the year. Connected with this question of seasonal variation in the malarias is that of the course taken in the natural disinfestation of the blood in cases of infection with *P. falciparum* and those of *P. vivax*: Does spontaneous cure occur more readily in the former than in the latter? The collection of evidence on this point requires the closest attention to the series of paroxysms in the malignant tertian cases, which, of course, cannot be allowed to run on to pernicious manifestations. Possibly the observations could only be made with safety in cases of both infections acquired in endemic areas transferred to non-malarious hill stations. The spontaneous natural disinfestation of all forms of malaria is what happens to the many millions of cases in India who never receive quinine treatment.

The writer doubts whether quinine is more specific in malignant tertian infection than in that of benign tertian. It is possible that in benign tertian the embryonic or latent parasite has developed the instinct of lying low in the presence of a poison (quinine) to a greater extent than the corresponding form of the malignant tertian organism. Under the effects of quinine, gametes in benign tertian are rendered impotent, while those of *P. falciparum* are not. Quinine rapidly removes all forms of benign tertian parasites from the surface blood, but malignant tertian crescents continue for some time. Under proper quinine treatment cases showing crescents are reduced 50 per cent. in a fortnight (J. W. W. STEPHENS).

Latitude.—The extreme latitudes within which malaria has been met are 60° N. and 40° S. India lies wholly within this zone.

II.—GEOLOGICAL AND OTHER RELATIONS OF MALARIA IN INDIA

The extent to which the water table rises, either locally or generally, above the surface of the soil, and so produces collections of surface water forming appropriate anopheline breeding places, constitutes the dominant feature in the considerations now to be adduced.

Telluric relations of malaria.—In connection with malaria the degree of porosity of the soil is of great importance, whereas the actual geological constitution and proportion of animal and vegetable constituents are of no significance. A soil that permits its contained water to drain rapidly, or that quickly absorbs such water, is unfavourable to malaria; one that holds up its surface water in small collections, such as small lakes, ponds, pools, etc., and only gets rid of it slowly, fosters malaria. Hence rocky soils (except where full of holes and shallows which retain water) and deep sandy soils are not favourable to malaria; but a granite soil covered by a layer of clay or even porous earth may be associated with severe malarial fevers. Loose, porous, sandy, alluvial and argillaceous soils, deep loamy, marshy lands, with a substratum of clay affording capacity for the retention of water, and level countries presenting physical obstacles to underground drainage, are most favourable (during a moderately high range of temperature) to the development of malaria. Many alluvial soils, especially those most recently formed, are malarious, although they may not be marshy. Many alluvial soils have a flat surface, a bad outfall, and are in the vicinity of streams which may cause great variations in the level of the ground-water. Uneven mud-banks also, on the side of rivers and large streams, especially if only occasionally covered with water, may be highly malarious; this is the case with many rivers and with deltas and old estuaries. Vast tracts of ground in Bengal, and in other parts of India, along the course of the great rivers (Ganges, Brahmaputra,

[1] *Trop. Dis. Bull.*, Vol. 19, No. 2, Feb., 1922.

hill stations. Malaria is known to occur at 8,000 feet in Quito (Ecuador). The general statement holds good, however, that the higher we ascend the less are the chances of a place being malarious, because the physical, telluric and climatic conditions become more unfavourable to the development of mosquitoes. Given suitable conditions, mosquitoes can thrive at high levels. "Nevertheless the reported existence of malaria in localities which, from general geographical conditions, might be expected to be free from the disease should always be carefully investigated, for relapses may occur in any climate and under a great variety of conditions."[1]

III.—Relation of Marshes and Places Simulating Marshes to Malaria in India

One of the oldest beliefs is that marshes have an intimate relation with endemic malaria: its earliest name, "marsh poison," indicates this. In ancient times marshes were associated with "ague," and drainage of marshes with reduction or even disappearance of ague. In the Middle Ages malaria was connected with marshes and swampy, low-lying areas, where mists and vapours ascended: the disease was believed to be due to breathing this humid atmosphere. Later, Lancisi (1718) connected marshes with gnats; these insects, he thought, might introduce with the proboscis the putrefying organic matter and animalcules of swamps. The French call the malarious process *paludisme* (L. *palus*, a marsh), and malarial diseases are frequently called *maladies palustres*, or marsh diseases.

Marshes, swamps, *jheels*, etc.—In India the inhabited regions adjacent to swamps, marshes, *jheels*, lakes, ponds, and other places simulating marshes, are practically always malarious; some of the worst foci of malaria in the Indian Empire, such as Assam, the Himalayan Terai, Bhutan Frontier, Manipur, the valleys of large rivers (Ganges, Indus, Jumna, etc.) possess such collections of water. Nevertheless there are swampy regions of vast area where no malaria is met with, indicating that other factors are necessary for the generation of malarial fevers; *per contra*, there are regions perfectly free from marshes and swamps which are endemic seats of malaria. In vast tracts of the Punjab there is a practical absence of marshes and swamps, the soil is dry for a large part of the year (the water being in many districts from 50 to 100 feet below the surface), yet there are various other sources of water such as the streams of the five great rivers, and the extensive areas supplied by irrigation. The same may be said of the highlands of Persia. The Upper Godaveri region is the most malarious in the Deccan, yet in it there is not an acre of marshy ground.

It is now well established that a marsh or swamp is not needful for the development of malarial diseases; yet in India marshes, swamps, ditches, and the low grounds subject to overflow by rivers, afford that conjunction of telluric conditions that is most favourable to malaria. A marsh at some distance, and in evidence, is often incriminated when the real cause of malaria is in the immediate vicinity of unhealthy houses, where, frequently, a close examination will prove the existence of many undiscovered or unexpected nurseries of anopheline larvæ. A plateau above a marsh is dangerous. Even the slope of a hill, a situation ordinarily to be recommended as a building site, when above a *jheel* or swamp, is likewise to be avoided, except when the wind is constant in the direction opposed to the slope, or from the slope to the *jheel*. Marshes produced by barriers of sand across streams form ideal breeding-grounds for Anopheles.

In some districts there is an extraordinary localisation of malaria. In one

[1] Thayer in Allbutt and Rolleston's *System of Medicine*, Vol. II.

Again, before we knew anything definite regarding the relationship between mosquitoes and malaria the writer made the observations shown in the following Table, regarding the relationship between the height of the subsoil water and malaria.

Table of Cases of Malarial Fevers treated in the Civil Dispensary of Chudderghaut during the years 1887–1889.

Year.	Number	Remarks.
1887 . .	37,000	High subsoil water level.
1888 . .	28,136	High but oscillating subsoil water level.
1889 . .	7,618	Uniform but low subsoil water level.

The large number of people that were affected with malarial diseases in the year 1886 led to inquiries regarding the causes of this malaria. The opinion arrived at was that it was due to the high subsoil water level, together with excessive "wet" cultivation within municipal limits. In the year 1889 wet cultivation was prohibited over an extensive area. The great disparity between the number of cases of malarial fevers occurring in 1889 and 1887 (7,618 and 37,000 respectively) is probably attributable to the uniformly low level of the subsoil water in 1889 and its high level in the year 1887.

"In the Dinajpur district I found a close relationship between high ground-water levels throughout the year and both high spleen and malaria death rates, while low ground-water levels were accompanied by much less prevalence of malaria. The great improvement in health in Algeria, following a lowering of the ground-water level by drainage, shows the value of this measure, which is about to be tried in some very malarial parts of Jessore (Lower Bengal)." [1]

The author's personal experience extending over thirty-four years, during ten of which he has been Health Officer in a locality where malarial fevers are endemic, is that there is an intimate relation between the height of the subsoil water and malaria. Indeed the literature and experience throughout India force on us the conclusion that a persistently low ground-water level, say 15 to 20 feet, is unfavourable to malaria; that a persistently high level, say 3 to 5 feet, fosters malaria; and that a level which fluctuates is liable to be most malarious.

Configuration of the ground.—This is highly important since it affects the manner in which surface water is disposed of. Hollows, ditches and all excavations without outlets, given other conditions, favour malaria; *per contra*, elevated sites, if they permit of rapid drainage, are unfavourable. It has for centuries been held that the "virus" of malaria does not ascend much above the level of the ground. In the medical literature of India of the last century one frequently comes across the phrase, "malaria loves the ground."

Altitude as affecting malaria.—The temperature drops 1° F. for every 300 feet above sea-level, and at high altitudes is too low for extensive anopheline breeding. Winds and ready drainage are also against it. But whilst for such reasons malaria is seldom met with at great altitudes, the old hard-and-fast rule that malaria does not occur by initial infection beyond 4,000 feet in India is certainly incorrect. The writer has proved the coexistence of malaria-bearing anophelines and malignant and simple tertian fevers at heights well above this, an observation which has recently been confirmed for certain

[1] Sir LEONARD ROGERS, *Fevers of the Tropics*, p. 203.

rice cultivation is unhealthy or innocuous. A rice-field under irrigation might be regarded as a type of swamp or marsh. The varying physical states of the soil in *paddy fields* is precisely such as we should expect to find associated with a prevalence of malarial fevers, they have the characters of marshes—alternately saturated with water and drying up. It is an important point, therefore, to decide the distance paddy fields should be from inhabited places, towns, barracks, etc. Amongst medical officers in India opinion is in favour of making this distance as great as is reasonably possible. Personally the writer considers that rice cultivation should not be permitted within 1,000 yards of towns and cantonments in India. In many towns in India rice-fields dovetail into the town. In Italy rice-growing is not allowed within five miles of towns. Rice cultivation is inimical to health in certain circumstances. In India, without adequate subsoil drainage, it is undoubtedly injurious to the health of the cultivators, and will continue to be so under existing agricultural methods. The healthiness or unhealthiness of a rice-field depends to some extent on the amount of water available for irrigation. Revenue Officers in India used to classify these fields as "one crop," "two crop" or even "three crop" fields. It might perhaps be safe to say that "one crop" cultivation is almost certain to cause malaria in the vicinity; that "two crop" cultivation is less dangerous, and that, other causes being absent, there is much less malaria in the vicinity of "three crop" cultivation.

As stated, some rice-fields are in very malarious places, in others the malaria is mild or altogether absent. The writer observed this in 1911 in Lower Burma. The flatter the country, and the more it was covered with water, the lower was the malaria rate. Generally, however, in every rice district in valleys, and at the foot-hills, the malarial incidence was high. Anophelines, in some places several species, can be found breeding in the majority of fields. In many of these instances none of the species found are vectors of malaria; in others one, two or even three species of malaria-carriers are present. This may be the explanation of some rice-growing areas in India being exempt from malaria, and others not.

Rivers and streams.—A river is not a straight sheet of water with a uniform flow from the mountains to the sea. Some of the large rivers of India and Burma pass through several countries, the same river often wandering from regions of perpetual snow to those of torrid heat, in any of these regions changing its character to become narrow and swift like the Indus and Jhelum, or broad, swampy and sluggish like the Ganges, Brahmaputra, Irrawaddy, Godaveri and others. A river may therefore have varying degrees of intimacy in its relations to malaria, as may be seen in tracing any large river from its tidal delta to its origin in mountain springs.

Clear mountain streams at the foot-hills are among the best breeding places for Anopheles, and in India are nearly always associated with paludism. Slow-running streams with marginal eddies and with bowers of shrubbery or branches of trees sheltering the water from the direct rays of the sun form excellent breeding-grounds for anophelines, and the deltas of rivers and drying-up river-beds are specially favourable.

Floods and inundations.—These, when receding and drying, are specially favourable to mosquito-breeding, and may cause intense and widespread anophelism. These conditions are usually (but not invariably) associated with other factors encouraging endemicity or even epidemicity of malaria. The malarial sanitarian in India dreads subsiding floods; some of the worst epidemics of malaria have been caused by them. The influences of such subsiding floods are often carried on to the following year, increased and persisting

instance, in Hyderabad (Deccan), the writer found that mild malaria had gone on for years in a group of villages, while in others less than a mile away it was almost absent. The only apparent difference was the presence of a limited marsh kept up by the waste from the weir connected with a large irrigation tank (Husain Saugor) near the former, with no breeding places in or near the latter. But striking localisation may be encountered without any established reason. The interior of a city or town may be fairly free from malaria while the outskirts are highly malarious; this is the case with Calcutta, which is surrounded by extensive marshes and rice-growing country. At the foot-hills of the Himalayas, and often extending on the plains for miles parallel with the hills, are extensive marshes. Towns, villages and houses situated in this marshy zone are malarious, sometimes intensely so. Outside this zone conditions may be comparatively healthy. The same holds good regarding a large number of towns in India, especially those under even moderately efficient sanitary control. There is one factor common to most of these towns: *A. subpictus* is the predominating species of Anopheles, and it has been suggested that this predominance may in some unknown way exclude other species (but see section on PREVENTION OF MALARIA IN TOWNS, PART III, pp. 365–373).

Irrigation canals.—The average amount of land watered annually by constructed irrigation canals in India varies from 26,000,000 to 28,000,000 acres. As a source of anophelines these are very important in India. Some anophelines, especially *A. fuliginosus*, breed in running water and, for these, irrigation channels are favourite nurseries. Irrigation channels not only breed mosquitoes, but, by seepage, the soil round them becomes sodden, and collections of water form in the irrigated area.

Irrigated lands.—These are a source of malaria, particularly when neglected. Irrigation canals supply vast tracts of cultivated land in India. In Manipur, and certain districts in India, all the *jheels* and rice-fields are connected by small canals, and in these anophelines are found to breed in myriads. Bengal, which is highly malarious in some districts, is richly irrigated by a system of canals which arise from both sides of the annicuts or weirs, thrown across rivers, distributing water during the dry season to the paddy fields.

Malaria is more persistent in its prevalence, more virulent, and therefore more fatal in its results, in the canal-irrigated tracts than in the country not irrigated, unless the districts are naturally very moist. "Indeed, nothing can be more marked as a rule than the difference in the aspect of the people who live where the well-water is found at more than 80 feet from the surface, and where it is found at less than 15 feet." "For eight months of the year, when all the country is dry, away from the canal-irrigated or moist terai countries, it is unusual to find a case of ague in any village; for four months of the year, when all the land and air is moist, it is difficult to find any village in which persons are not suffering from ague, and this suffering is more general, more lasting and fatal, as the rainfall of any year is greater or late, so that its drying up is delayed." [1]

Rice cultivation.—The methods used in growing rice call for flooding the fields for several weeks, and this has to be maintained during the active growing period of the rise, the surface being covered with from 4 to 6 inches of water all this time. The conditions present form ideal intensive nurseries for most species of Anopheles—quiescent water, shade of the growing crop, and plankton. Until a few years ago authorities were not agreed as to whether

[1] F. N. MACNAMARA, *Himalayan India*, pp. 413 and 370 *et seq.* Also *Report on Malaria in the North-West Provinces and Oudh*, 1866.

this section we have seen that the presence of water in conditions suitable for the breeding of mosquitoes is the dominating factor of malaria. Malaria exists in the Sahara only at oases; at some of these, *e.g.* Biskra, it is severe. In nearly all towns and practically all villages in India the cheap houses and huts are constructed of mud walls, or mud dried bricks or burnt brick in mud mortar. This mud is obtained by excavating a pit close to the house or hut to be built: these pits, once created, usually remain permanently, and contain water for the whole or part of the year.

Deforestation.—The process of deforestation and the neglect of land previously well cultivated are well known to be associated with malaria.

Man-made malaria.—It is clear from what has just been written that the difficulty of reducing malaria in India is increased by the continual creation by man of fresh breeding places for mosquitoes. Any work, whether it be the making of railroads, public highways, canals, towns, barracks, houses, etc., which leaves a trail of malaria behind it, is bad engineering. The sooner all concerned recognise and forbid this, the sooner will all man-made malaria disappear. It is not uncommon in India to see a municipality spending considerable sums of money in filling in or draining pools, ponds and tanks while at the same time railway engineers at another part of the town are building railway embankments, creating borrow-pits, or damming back the subsoil water by failing to build their culverts sufficiently deep to carry it off (see Fig. 99, p. 350).

The foregoing is a description of the contributory conditions which foster malaria; they are, however, not necessarily associated with it; we have vast tracts of the earth's surface in which they are all present—high temperature humidity, marshes, etc.—yet in which malaria is absent. "Some of these conditions act on the source or carrier or receiver of infection; others affect all of them directly or indirectly. A factor which by its action may promote malaria can at the same time, by its action in another part, tend to lessen the disease." Rainfall favours the multiplication of Anopheles, but promotes agriculture and prosperity; the last helps in recovery from malaria, and decreases both its prevalence and severity by increasing resistance. Again, what promotes malaria in one district may remove or abate it in another, *e.g.* floods in marsh lands.

From all these statements it will be obvious that the contributory endemiological and epidemiological factors regarding malaria almost completely coincide with the mosquito-malaria theorem referred to later on. There are differences in the manner in which these individual factors operate in different places, and the exact relationship of soil, temperature and rainfall to malaria can only be worked out by extensive inquiry regarding their effects in particular places.

IV.—Relation of the Anopheline Population to Malaria

There is much evidence to show that the severity of malaria has a direct relation to the number of infected anophelines; any circumstances increasing the latter intensifies the local malaria.[1]

The infected anopheline feeds regularly for a number of consecutive nights, and in this way probably infects several people. Further, it may infect more than one person on the same night. Hence a comparatively small number of anophelines are capable of causing much malaria. In the British troops' barracks, Maymyo (Burma), in the autumn of 1912, with abundance of help, the writer succeeded in getting only 47 anophelines in 6 days; of these 22 per cent. contained sporozoites. In the British Artillery barracks (provided with electric

[1] Sir Ronald Ross discusses this aspect of malarial epidemiology clearly and logically in his *Prevention of Malaria*, 2nd Ed., Chap. v.

anopheline breeding co-operating with the vast number of cases of residual malaria. But there have been flood years in India in which there was no such epidemic increase of malaria. The question is evidently much more complicated than appears on the surface.

Bhils.—These are large natural depressions in the land filled with water and corresponding with our lakes. For the most part they retain a connexion with a river continuously or only during the rains. They form extensive breeding places for mosquitoes, and are very numerous in some provinces, especially Bengal and Assam.

Tanks.—These form one of the largest classes of breeding places of anophelines in India. They are found around and in almost every town, station, cantonment, village and hamlet. A large number of tanks fill during the south-west monsoons, but after the rains, begin to dry and become sources of malaria. Accordingly, whilst a temporary camp may be formed near a full tank, a permanent camp or building should never be so located, nor placed near marshes, banks or beds of rivers which are drying.

Irrigation storage tanks.—In the Deccan and Southern India there are also large numbers of storage irrigation tanks, they are not much favoured by malaria-carrying mosquitoes, and they are usually at a distance from towns and villages.

Ravines.—In India ravines are always unhealthy, especially if covered with jungle, close brushwood, etc. The mouths of ravines are specially dangerous places. The summits of ravines are at times also malarious, especially if only a few hundred feet high.

Ditches.—Next to irrigation canals, in the production of malaria, may be enumerated *ditches* surrounding towns, cities and forts, and the badly graded ditches in flat districts generally. Ditches surrounding towns, either when they become stagnant, or when they are drying by continued heat, become the source of malaria in the same way that marshes do; they are often the cause of disease to the inhabitants for whose protection they were made. Ditches of whatever description, whether used for the protection of towns or of camps, or for draining the soil, unless carefully looked after, are in India productive of malaria, particularly when they are drying.

Pools, ponds, etc.—The influence of *pools* in the production of malaria must be evident from what has already been advanced. Rain-water pools and small collections of water, subject to periodical replenishment, are specially favourable to anopheline breeding. Clear pools in a clay area, especially if provided with shelter by marginal shrubs or trees, may be found swarming with anopheline larvæ.

Borrow-pits.[1]—These are ubiquitous in India. It is rather doubtful if borrow-pits are so popular with mosquitoes as is generally supposed. Freshly created ones are certainly not; the water, if there is any, is usually muddy, and there is, as a rule, an absence of vegetation in the water or at the margins. The risk commences when the water in the borrow-pits contains aquatic plants and the margins are covered with vegetation. One of the great causes of the increase of malarial fevers in certain districts appears to be the general construction of roads, railways, irrigation tanks and irrigation canals, which obstruct the outfalls of the subsoil water in the one case, and keep the soil damp and water-logged, and in many districts marshy, in the other. Throughout

[1] Borrow-pits on roads and along railway lines are rectangular excavations running in a continuous chain on one side (or both sides) of the road or line, usually having a column of earth near the centre of each pit, to show the depth of the earth removed and enable the contractor to calculate the quantity of earth used in the roadway or railway embankment.

links which represent this necessary close association can be cut by taking the steps to prevent the insect carrier having access to the particular human beings concerned. In nature the degree of association varies in different localities and circumstances, and when other factors remain constant, the amount of malaria in the locality varies accordingly."[1] It may require the closest attention to each of these factors to enable us to discover where the association is, and in the working out of such problems interesting practical points are sometimes brought to light. In all circumstances it will be found that the initial amount of malaria in a locality is of paramount importance.

E.—PERSONAL PREDISPOSING CAUSES OF MALARIA IN INDIA

Age.—Malaria attacks all ages but most frequently children under ten years. The very old and very young (infants under three months) are less frequently affected with malaria in endemic districts. The former have probably acquired a certain degree of immunity to the parasite, the latter have not had time to get thoroughly saturated with malarial toxins and establish a reaction. The writer has, however, seen large numbers of infants of six months of age in malarious districts with splenomegaly, and it is well known that a considerable number of them die directly or indirectly from malaria during the first year of life. Children in endemic areas are, to ten years of age, much more frequently and seriously affected with malaria than adults. This arises from their thinner and more delicate skins being more vulnerable to the attacks of anophelines, the relatively large number of sporozoites injected in proportion to their body weight at each infection and re-infection, their scanty attire and comparatively large exposed surface, sounder and more prolonged sleep, inability to defend themselves against mosquito bites, and the absence of acquired immunity. In hyperendemic and severely endemic areas, some degree either of tolerance to toxins or of actual immunity is acquired between the ages of five and six years.

Sex.—The male sex is attacked more than the female on account of greater exposure to attacks of anophelines and various subsidiary causes that lower resistance, such as more severe toil and effects of inclement weather. Sex itself, however, has little to do with the incidence of malaria; when both sexes are equally exposed to infection they are equally infected. It is possible to show that where women are largely employed in manual labour like men, they are largely infected. In one instance on a large canal work (the Bari Doab in connexion with the Ravi and Beas Rivers), where about 2,800 women were employed, the writer investigated the local malaria and found 910 with malaria parasites in their blood, or 32·5 per cent., and of 1,700 men on the same work at the same time, there were 551 harbouring parasites, or about 32 per cent. Manipur, which is about 3,000 feet above sea-level, consists of a valley 30 × 10 miles, irrigated throughout by intersecting canals; it is highly malarious; the children are practically all infected with malaria, whilst the men and women, who are throughout equally exposed, are affected to only a comparatively small but equal extent.

Race.—Native adults resident in malarious places are less liable to malarial infection than Europeans and immigrants from non-endemic areas. They acquire more or less immunity *early in life. The* blood of a large percentage of native children is inhabited by the parasites of malaria. Newly arrived Europeans in malarious localities in India are specially liable to malarial infection. If exposed to malarial influences for some time without suffering from

[1] S. P. JAMES and S. R. CHRISTOPHERS in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. II, p. 1515.

fans), Bareilly, in the autumn of 1909, under the same conditions, he got only 50 anophelines in 4 days, with 13 per cent. infected. In both instances malaria was very prevalent among the troops. In this observation a point overlooked at the time is that it is highly probable that more than half these cases of malaria were relapses, and not fresh infections from current attacks of Anopheles. It is only during the last few years that statistics regarding the relative frequency of relapses to new infections have been collected in the Army in India (see pp. 13, 14 and Appendix I.). There are many places in which infected anophelines are few but malaria common, and *vice versa*.

Sometimes with large numbers of known malaria-carrying anophelines there may be little malaria, although there is a sufficient number of malaria cases to expect a high malarial incidence. Why this is so we are not able to explain. It indicates that the prevalence of malaria-carrying Anopheles is only one of the factors in the spread of malaria. As S. P. James and S. R. Christophers remark: "The amount of malaria in a locality will vary in accordance with variations in the number of Anopheles only when all the other factors remain equal and constant."[1]

An increase of the general mosquito population in an endemic area may be associated with a fall in malaria. In one set of observations it was demonstrated that with 200 to 500 mosquitoes per house, 6 to 8 per cent. contained human blood, whereas in another set, with 1,500 per house, only 3 per cent. or less contained blood. This paradox of abundance of malaria and few Anopheles and *vice versa* is most curious, profoundly interesting endemiologically, and calls for interpretation. The Malaria Commission of the Royal Society (India, 1902) found that at Ennur (Madras), in a fortnight, they could collect only about fifty Anopheles, with 2 per cent. infected, whilst in other places with thousands of *A. culicifacies*, adults and larvæ, the malaria was *nil*.

In our malarious cantonments the disease is less prevalent in European troops than in the local indigenous inhabitants, because British Troops' barracks are in most stations situated at a distance from the main source of infection—the Indian civil community, especially Indian children—and because they are perpetually under medical observation and, when necessary, treatment. Where such separation cannot, for military reasons, be carried out the disease is more prevalent in European troops than in the local inhabitants. Examples of this are the Delhi, Lahore and Peshawur Forts.

In many towns and cantonments in India malaria is kept within moderate bounds by the strenuous efforts of the sanitary and other officials, and by carrying out a definite, practical, anti-malarial campaign. In some, however, the margin of safety is exceedingly narrow. In others, where there is no definite campaign in operation, there is no margin of safety; and the addition of another factor fostering malaria, such as the accession of a large body of non-immunes, or the immigration of large numbers of Anopheles that are natural carriers of malaria, will lead to hyperendemicity.

Whilst the subject of anophelines is of extreme importance in the study of malaria, it will be seen that there are other highly important factors which determine the prevalence of malaria in a locality, and it is necessary that we should be able to give the exact relative values of these factors in an investigation. We unfortunately find only too many instances in which it is not possible to explain the relationship of the individual factors to each other and to the whole subject of local prevalence. "In some the explanation lies in a knowledge of the degree to which there is close association between the human host, the insect carrier and the susceptible population. By artificial means the

[1] Byam and Archibald's *Practice of Medicine in the Tropics*, Vol. II, p. 1513.

under which they live—huddled together in small *chappar* huts, scantily clothed, with meagre food of small nutritive value, and exposed to night chills. This is a very prevalent combination of conditions amongst large gangs of workmen in India.

The recently published *Report on its Tour of Investigation in Certain European Countries* of the Malaria Commission of the League of Nations lays great stress on the house as the site of infection in nearly every case, and housing plays an essential part in the Italian anti-malarial *bonification*.

State of education.—The incidence of malaria is considerably higher among the uneducated, labouring and agricultural classes than among the educated, who have acquired some knowledge of sanitation, personal hygiene and the nature and methods of prevention of malaria.

Delayed recovery rate.—Unfavourable economic conditions affect the length of time malaria infection lasts; without quinine treatment and suitable feeding spontaneous cure is a lengthy process, and even with these, if the patient has been living in poverty and squalor, it will take longer than under ordinary conditions. This may be called the *delayed recovery rate*.

Lowered resistance.—Exposure to cold or excessive heat, a wetting in the rain, over-eating, fasting, exceptional physical fatigue, hardship, privation, worry or mental strain, a surgical operation, etc., anything which lowers the resistance and vitality of persons with latent malaria predisposes to an outburst of paroxysms. At the commencement of the annual manœuvres we find a rapid rise in the incidence of malaria among troops who have been quartered in malarious stations and performed comparatively light peace-time duties in cantonments in India. The same happens in troops at the early stage of campaigns on the North-West Frontier and elsewhere. On the other hand, the disease sometimes breaks out in persons in seemingly good health leaving an endemic area for a health resort, whether on the hills in India or en route to Europe.

Previous attacks of malaria.—Previous attacks of malaria predispose to further attacks from slight causes. A simple catarrh, indigestion, a hard day's work, a cold bath, and even change to a colder and more salubrious locality, may bring on an attack. Most of such cases are relapses and not new infections. Old residents in malarial districts, especially Europeans, are very susceptible to changes of weather. Minor causes harmless to new arrivals may give rise to a fit of ague in an old resident. Occasionally relapses are stimulated by "water cures." Men sometimes get their first relapses at Carlsbad after leaving India—the baths in some way re-invigorating latent malaria parasites.

Pregnancy and malarial infection.—Pregnant women acquire malaria as freely as the non-pregnant. The later the infection occurs during pregnancy, the greater the liability to miscarriage.

Menstruation and parturition.—Menstruation commonly excites a relapse; it may be accompanied or followed by a bout of paroxysms. In exceptional cases each series of paroxysms begins at this time. Parturition may have a similar effect.

Occupation.—This is a factor predisposing to malarial infection only in so far as it exposes to the attacks of infected anophelines. Those employed in excavating soil in malarious places, in building railway lines, roads, etc., and camping on the sites where these excavations take place, are especially predisposed, because they dwell in the midst of the breeding grounds of anophelines. But in these cases hard work, exposure and defective diet are predisposing causes; many of them are relapses. Work in rice-fields, in

malarial fever, they may acquire a certain small degree of immunity. In no circumstance does the European in malarious places acquire complete immunity or undergo complete acclimatisation. MAUREL states, regarding the white people of French Guiana, that he could not trace a single white family back more than four generations, and definitely declares that no immunity is acquired by the Caucasian race. Eurasians are more subject to malaria in endemic malarial areas than natives, in this susceptibility following their European progenitors. This observation was originally made by RONALD MARTIN and has been repeated by many experienced medical officers in India. In the early days of building the Panama Canal it was observed that, although Anopheles abounded, the indigenous community escaped evidence of malarial infection to a remarkable degree; new-comers were constantly infected.

Partial immunity is very common among the people of India; vast numbers of them contain malaria parasites in the blood for long periods and yet suffer no appreciable discomfort, until for some reason their resistance is lowered and paroxysms set in. Such partial immunity of most Indians is not attributable to exemption from mosquito bites; they are probably bitten more than Europeans as more of their pelt is exposed to attack, especially in the case of children.

Apart from constitutional peculiarities, individual predisposition to malarial infection is met with, which may in part be explained by the fact that some people are more attractive to mosquitoes than others. Indeed, it is the case that mosquitoes will not bite some people. The writer shared for a year the same bungalow with one such person, a European military officer, who never needed a mosquito net nor prophylactic quinine, and in a highly endemic malarious station never became infected. He watched him throughout the malarial season with much curiosity, but there was nothing discoverable to explain his distastefulness.

Immunity.—This subject is dealt with separately at the end of this section.

Alcoholics are more susceptible to malaria than the temperate, and in them malaria is more severe.

Defective hygiene.—Defective hygienic conditions are important predisposing causes. Houses that are small, damp, dark, ill-ventilated and dirty are specially favoured by mosquitoes. The small, damp, thatch or bamboo, windowless huts of most villages are examples. Large houses with lofty rooms, good ventilation, abundance of light and all sanitary needs considerably reduce the possibility of infection.

The poorest classes are the greatest sufferers from malaria, because they are not well nourished, and they are never protected from the attacks of mosquitoes. This is often seen where the poorer classes of Indians, living in the same locality as well-to-do Europeans, suffer considerably, the latter often only slightly, because of the better hygienic conditions under which they live, and the measures they take to prevent the bites of mosquitoes.

An adequate amount of suitable food is an important factor in the development of immunity. Where underfeeding and hyperendemicity coincide in rural India, there we get the largest numbers of greatly hypertrophied spleens in children and malarial cachexia in adults.

Because of the improper and scanty food, miserable housing, insufficient clothing to protect from chills, excessive work, etc., the ordinary village peasants, notwithstanding the immunity they possess, fall victims by the million to malarial infection.

The enormous outbreaks of malarial fevers that occur amongst coolies on canal irrigation works are largely fostered by the unwholesome conditions

factor, however, presents difficulties. In response to such tests as were used in West Africa a negro with 3,000 worms appeared just as fit as one with three. The same holds good in parts of S. America. The general and special effects of ankylostomiasis as a complication of malaria have not been worked out.

Place of residence.—Residence in an area with human malaria-carriers (pp. 51–54) and anophelines capable of transmitting the disease is a dominant factor in predisposing to malaria, as is living in an infected area with meteorological conditions of air, moisture and temperature particularly suitable for the development of the parasite in the anopheline vector, and with suitable breeding places for their larvæ. Warm, marshy places in the wet season are ideal.

Scanty and thin clothes.—The scanty clothing worn by the masses, day and night (and even much of that thin cotton, which the mosquito can readily pierce), exposes a large surface of the body to attack. Most of their children, up to the age of five or six, live naked, a fact which partly accounts for all of them acquiring malaria at an early age, and for their constant re-infection. The European style of dress is much more protective against mosquitoes.

Time of day most dangerous.—Owing to the nocturnal habits of most Anopheles the risks of malarial infection are greater after sunset, during the night and in the early morning than during the daytime. Houses darkened to keep out the day heat and brightness and glare bring some species of anophelines out of their hiding-places to feed on man.

Other factors.—Some factors bring the source of malaria, the carrier and the receiver of infection, into the required intimate relationship with one another. In India we find places in which the presence of many human malaria-carriers and abundance of Anopheles is not associated with a corresponding prevalence of *fresh* infections. Also districts in which there are only a comparatively few malaria-carriers and few Anopheles but a widespread prevalence of fresh infections. In the first group—*paludismus sine malaria*—there are the required conditions but little malaria, in the second group—*malaria sine paludismo*—there is much malaria but no conspicuous existence of the required conditions.

It should be remembered that the coincidence of a marked decrease in the number of anophelines without decrease in the incidence of malarial fevers is quite explicable when the immigration of previously infected persons continues, or when by any means the source of infection is increased. "The prevalence of the source of infection is a factor of equal and sometimes perhaps of greater importance than the prevalence of anophelines" (S. P. James).

With reference to the various personal predisposing causes of malaria dealt with it must be stated that the evidence in connexion with the effects is rather scanty; some of the factors included are merely traditions handed down by authors and copied from one generation to another. It is obvious that there is much scope for exact observation in this field.

F.—IMMUNITY TO MALARIA AS MET WITH IN INDIA

Immunity is one of the most interesting subjects connected with malaria. Up to the present we are unacquainted with the mechanism by which it is brought about, but there are various highly ingenious speculations regarding it. In all probability the factors in operation are somewhat complex.

Immunity is here employed in two senses: (1) true immunity, or parasite-proofness, in which parasites will not survive in the host; (2) tolerance to the

deltaic areas of rivers, in low-lying marshy districts, in recently deforested land specially predisposes to malarial fevers. One of the most formidable instances of severe malaria of modern times illustrating this is the terrible havoc created, in part at least, by malaria amongst the workmen employed during the earlier attempts to make the Panama Canal. This is the more noteworthy when we contrast it with the reduction of malaria effected in the Panama Canal Zone by anti-malarial and anti-mosquito measures. It is probable that people following the above occupations acquire more speedy immunity than those whose occupation keeps them indoors. See section on RÔLE OF MAN IN THE DISTRIBUTION OF MALARIA, PART I, p. 45 *et seq.*

State of health.—All conditions enfeebling the body even temporarily, such as common colds, remaining in wet clothes, a wetting in the rain, severe bodily fatigue, excessive mental work, inadequate amount of sleep, excesses of any kind, excitement, defective and insufficient diet, drug habits, parturition, menstruation, minor illnesses of all kinds, injuries acute and chronic, surgical operations and defective dwellings, increase the susceptibility to malarial infection. Hence the advisability of using quinine under all circumstances liable to enfeeble the resistance to malarial infection. Similarly all bodily and mental depressions tend in some way to revive the vitalities of latent malaria parasites and bring about relapses; hence the necessity, once infection has occurred, of completely eradicating malaria parasites by a prolonged course of quinine.

There is no doubt that persons in good health are capable of throwing off a mild infection of malaria without presenting any clinical manifestations of such infection. This must constantly be happening in malarious districts even without quinine prophylaxis.

Impoverishment.—The food of the population is important in maintaining a condition of nutrition that will give the body a certain amount of vital resistance against the multiplication of malaria parasites, when these reach the blood. The question as to the best way of increasing the prosperity of the poorer classes of villagers is one deserving all possible attention. In this connexion it is necessary to say that a sufficient quantity of wholesome food can be ensured by the enforcement of a minimum wage for all labourers on all contractors and other employers of coolie labour. This would, of course, affect to a slight extent only village populations carrying on agricultural work, but it would affect a very important class of labourers through whom malaria is to some considerable extent disseminated and maintained in India.

Statistics issued by the Government of India show that there are approximately 146,000,000 cattle in British India, 73,000,000 males and 73,000,000 females; there are 65 bovine cattle to 100 acres under cultivation, and 61 bovine cattle to every 100 of the human population. The maintenance of these enormous numbers of animals creates a pressing competition with man for the products of the soil, and is at least partly responsible for the economic stress. These animals, however, also cause a diversion of Anopheles from human beings, and this may possibly be responsible for keeping the malaria in India within limits. There is always in an agricultural population, even in those living near subsistence limit, a fair margin of resource which enables them to resist in a remarkable way temporary stringency.

In all probability the percentage of ankylostome infestation in India is over 90. When this and malaria both call on the marrow to replace lost red corpuscles the balance between loss and repair is more likely to be upset than when malaria acts alone. In its usual indirect way hookworm infection must be looked upon as increasing the mortality from malaria. The hookworm

to result, not merely in a considerable degree of tolerance, but also to some extent in true immunity. In a malaria survey of, say, 100 children between four and six years of age, in an ordinary endemic malarial town or cantonment, it is certain that the blood of some who are quite free from paroxysms will have malaria parasites and enlarged spleens. This tolerance becomes strengthened by further infections and re-infections up to the age of ten to twelve years. Yet all this time these children have been what we may call *healthy malaria-carriers*, that is, they give infection to susceptible people but do not appear to suffer much from malarial paroxysms themselves. After this age, however, their immunity appears to take on a more active form, and then malaria parasites are no longer to be found in their blood, the splenic enlargement is greatly reduced and may disappear. S. P. JAMES[1] gives most striking charts of this (Figs. 1 and 2). The writer's experience completely coincides with his.

A small percentage of adults in endemic areas have pyrexial attacks off and on during the malarial season without knowing it. The writer has proved this in Indian troops by taking the temperature on parade at medical inspections. During these inspections he invariably felt the axilla of one side. Whenever doubtful as regards fever he had the temperature taken. In September, 1917, at Jhelum, in one regiment 721 strong at one inspection he found five cases with temperatures above 101° F.; all had benign tertian parasites in the surface blood. In such cases parasites are usually scanty, but these men become infective to their comrades periodically.

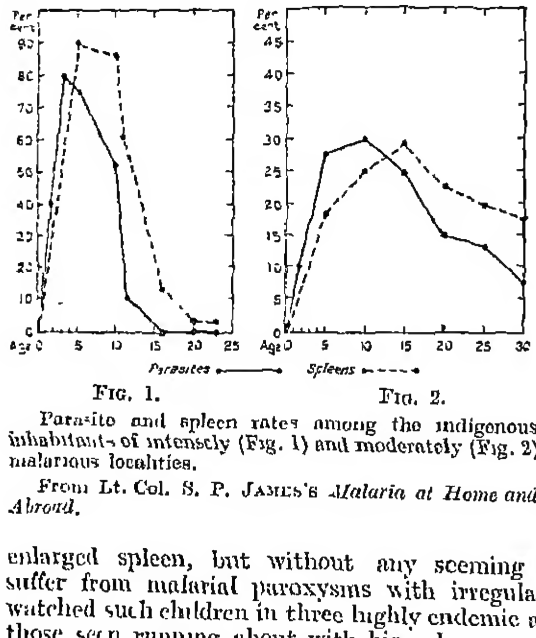


FIG. 1. FIG. 2.

Parasite and spleen rates among the indigenous inhabitants of intensely (Fig. 1) and moderately (Fig. 2) malarious localities.

From Lt. Col. S. P. JAMES'S *Malaria at Home and Abroad.*

Children are met, in endemic malarious districts, with parasitic infection and enlarged spleen, but without any seeming serious inconvenience. They suffer from malarial paroxysms with irregular periodicity. The writer has watched such children in three highly endemic areas for months and found that those seen running about with big spleens were the survivors; from infancy they had suffered from bouts of serious illness. If in malarious places we find children of from eight to twelve years comparatively healthy, the mortality up to five years of age will have been very high. "It has been observed in India that the death-rate of children in areas of high endemicity is twice as high as in non-malarious areas, and that such areas can be mapped out on the basis of the total mortality of children between two and five years of age." The late Lt.-Col. W. H. KENRICK, I.M.S.,[2] who made a comprehensive and close study of this subject in the Central Provinces in India, noted that, while deaths from malaria in adult Indians are due usually to complications with some added disease, children are killed by the *intensity of the parasitic invasion.* He recorded the following as being a frequent history of fatal cases of uncomplicated

[1] *Malaria at Home and Abroad*, p. 15. [2] See also Appendix VI—1.

ill-effects of parasites which do in fact persist, sometimes for years, without producing malarial attacks.

Against malarial infection there is no absolute immunity, hereditary or acquired. The parasite may remain in the system for long periods; latent parasites are of frequent occurrence in adults of endemic districts. It is stated that dark-skinned races, living in malarious regions, possess a relative immunity to malarial infection. This is explicable as an acquired immunity, the result of frequent infections in childhood. On the West Coast of Africa indigenous negroes undoubtedly possess a high degree of immunity to malaria, whereas imported negroes are moderately susceptible to infection. When malarial fevers first occurred in Mauritius in 1867 all the negroes are said to have escaped it, while the indigenous population suffered severely.

Acquired immunity.—The relative immunity of inhabitants of endemic areas is acquired and not inherited. We find in such areas a high percentage of the children harbouring malaria parasites in their blood and, in ordinary years, comparatively few adults with parasites. Prolonged residence in malarial districts gives rise, in those who survive malarial infections, to a degree of relative immunity. There is no doubt that recurring attacks ultimately render the individual less prone to infection. The explanation may be that the malarial toxins bring about some changes in the human economy which render it less liable to further attacks. In other words, we get a condition in which, after repeated attacks of malarial fever which have become less and less severe, there is established a spontaneous and more or less permanent cure. This is brought about more rapidly in some cases where quinine has not been used (Koch). This immunity may endure for years, but any condition lowering the vitality or lessening the resisting power is liable to remove it. Loss of immunity often arises on going to a new locality. Some people are more resistant to the pathological effects of malaria parasites than others. Among Indian troops particularly it is noticed that even in severe endemic seasons a high but varying percentage of the soldiers escape illness. The barracks are not screened, and in many units mosquito nets are not used. It would be unreasonable to suppose that those enjoying this freedom from infection have not been bitten by malaria-carrying anophelines as their less fortunate infected comrades have. They have acquired immunity from many previous attacks.

Although there is no true racial immunity to malaria, yet in all races certain individuals are for unascertained reasons naturally immune. Some of them are not bitten by mosquitoes. In others, no doubt, infection with a small number of parasites is often overcome, largely through a vigorous phagocytosis. Resistance varies in different individuals, and in the same individual at different times.

Fortunately immunity to malaria is developed in the large proportion of people in endemic malarious areas in India, otherwise depopulation would be inevitable. If immunity, partial or complete, did not exist, the population of hyperendemic areas would, in the course of a few generations, be exterminated. The immune are but survivors; a high percentage of those born die in the early years of life without acquiring immunity. It is usually stated that immunity against one species of malaria parasite confers no protection against infection by another species; this is very improbable. At any rate, in India, during the earlier years of life, infection with both malignant tertian and benign tertian parasites takes place so repeatedly that in later years there is protection against both.

In very malarious areas a certain degree of immunity is acquired before the age of five. Prolonged intense infection in infancy and early childhood seems

the agencies concerned in the development of immunity in some individuals are stronger than in others, thus delaying or altogether preventing the onset of symptoms." [1]

Reserve, however, must be observed in applying these considerations to naturally acquired infection. YORKE and MACFIE invariably induced benign tertian malaria (41 cases) by means of Anopheles, but failed to do so in 9 of 70 direct inoculations. On the other hand, S. P. JAMES failed to infect on two occasions in which numerous sporozoites were subsequently found in the salivary glands. Since, too, as indicated below, quinine appears to act differently upon sporozoites and schizonts, it is well to be cautious in generalising regarding natural immunity upon evidence furnished by infection with schizonts instead of with the natural sporozoites. Experience in India appears to show that the number of non-immunes who would escape infection if bitten in the ordinary way is negligible.

One of the most comprehensive pronouncements on the question of the acquisition of immunity in hyperendemic areas published in recent years is that of Lt.-Col. S. R. CHRISTOPHERS, C.I.E., F.R.S., I.M.S.[2] The report refers to the labour force in three mining camps in which malaria was hyperendemic, and should be in the hands of all persons making malarial investigations of this kind in India. From this report the writer has taken the liberty of quoting the following paragraphs.

"*Malarial infection in children in hyperendemic areas.*—Among the 18 children of age 1–2 resident on the estate for at least 12 months the average parasite value was 12,084, and the infections encountered ranged from 83,000 to 140 parasites per c.mm.[3] Assuming that each child had the same history as regards cycles of parasites as the others, we may, for the purpose of illustration, make the following approximate estimate of what an individual child passes through. As 18 children examined at random at a given time had 5 infections of over 10,000 per c.mm., one child of these 18 is likely in 18 days, on an average, to have 5 such infections. Similarly, for 13 out of the 18 days it ought to have over 1,000 parasites per c.mm., and no day without parasites. The significance of these findings is further appreciated when it is considered that, as a result of counts of parasites in attacks among seamen, Ross and THOMSON (1910) fixed 200–500 in the case of *P. vivax* and 600–1500 in the case of *P. falciparum* as the number of parasites per c.mm. required to cause fever. From counts given by these authors it would seem that from 3,000–4,000 parasites per c.mm. were invariably associated with an attack, and a temperature rising to 103° F. or over. Taking even 5,000 parasites per c.mm. as a convenient test number for an infection sufficient to cause an attack, each of these children must be considered as under 'attack' conditions in respect to the number of parasites in their blood on 8 out of 18 days at least. Not only so, but the number of parasites would represent attacks of some severity. The highest count in the series is only once exceeded in Ross and Thomson's figures, and out of 30 attacks in the seamen, only 8 are as high as the next four higher in the children. This degree of infection, also, was not during the fever season when one might suspect it to be temporary, but at a time when malaria transmission was probably least active.

"There seems little doubt, therefore, that *this intense infection, that can only be described as continuous attack, with an average parasite count of over 10,000 parasites per c.mm., and lasting something like two years, is an essential feature of*

[1] W. E. DEEKS, *Prevention and Treatment of Malaria*, p. 3.

[2] *Enquiry on Malaria, Blackwater Fever, and Anchylostomiasis in Singbhum.* Report No. 1, Preliminary Investigation into the Conditions of the Bengal Iron Company's Mines at Manharpur, January, 1923. Abstracted in *Trop. Dis. Bull.*, Vol. 21, p. 285 *et seq.*

[3] The volume of blood examined was estimated by ascertaining the area of the preparation covered by the square aperture of the Ehrlich eyepiece with the combination of lenses in use.

malaria in native children: "An apparently healthy child has an attack of fever lasting seven or eight days. The child then appears to be quite well for two or three weeks, when there is another bout of fever, which is followed by another apyrexial period. The relapses now begin to occur at more frequent intervals and with greater severity. In the absence of quinine, unless the child succeeds in surviving until it has acquired a certain degree of immunity, death occurs, often with cerebral symptoms."[1] This corresponds precisely with the author's experience. It is a comprehensive statement of a tragedy that is being enacted year in and year out over extensive tracts in India, Assam and Burma. It is only in comparatively recent times that we have recognised the main source of malaria in India to be the infected indigenous children. This fact was originally brought to notice by Surg.-Maj. D. DEMPSTER, I.M.S., in 1846, and then for a long time lost sight of. Adults are a source of infection, but to a much less extent, and much less obviously, since they do not seem to be much incommoded by the infection in consequence of the relative immunity they have acquired by repeated attacks in childhood. The children of Europeans, though usually living under more salubrious conditions, are more susceptible to malaria than indigenous children, and in endemic areas very few of them escape infection.

There is considerable variation in the susceptibility of individuals to malarial infection; in other words, the protective and defensive agencies in the body of different people vary greatly. This difference affects the length of time after infection at which paroxysms begin; this time may be delayed days, weeks or even months. If the vital resistance is sufficiently potent the parasite or its toxin is destroyed and no paroxysms occur—there is immunity.

It may be remembered that recently it has been declared to be dangerous to interfere with the process of acquiring immunity by the use of prophylactic quinine unless the latter is maintained (see QUININE PROPHYLAXIS, PART III, pp. 282–290).

In connexion with the treatment of general paralysis by induced malaria, several important points have been brought out regarding immunity. Of a series of 98 cases inoculated with malarial blood (containing benign tertian parasites) 9 failed to respond to the first inoculation and, in a few, repeated inoculation proved innocuous. VAN LOON and KIRSCHNER of Batavia, from their experience connected with induced malaria cases in the treatment of general paralysis, report that "a great percentage of the patients who had lived in the tropics from their birth, and who were repeatedly (4 or 5 times) intravenously, and afterwards also subcutaneously, inoculated with relatively large quantities of benign tertian blood, appeared to be absolutely immune; others fell ill, but slightly only, and recovered spontaneously after a few attacks." It would be interesting to ascertain whether similar immunity exists in general paralysis in endemic malarious places in India. Of the 98 cases referred to above the parasite appeared in the blood in from 6 to 20 days, and the fever occurred in all cases about the same time, yet in a few cases coming on in advance of, or following by a day or two, the finding of the Plasmodium. In 4 of the 6 inoculated with *P. falciparum*, parasites appeared in the blood from the 10th to the 21st day after inoculation, in 1 on the 44th day, and in 1 on the 54th day. Similar observations have been made in over a dozen groups of cases.

Again, although identically the same quantity of actively infective malarial blood containing quartan parasites was injected in different persons the incubation period varied from 16 to 54 days.

Evidently different degrees of resistance exist to both quartan and benign tertian infections; it takes a longer time in some persons than in others after infection to develop sufficient parasites to produce paroxysms, "or what is much more probable,

[1] Lt.-Col. W. H. KENRICK, quoted by JAMES and CHRISTOPHERS in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. II, p. 1619.

conditions which to the newcoming child mean intense, almost continuous, heavy infection, the adult lives infected, but without suffering illness. It is necessary to remember, however, that the conditions here dealt with refer to the non-fever season. There is some reason to believe that, in malaria, immunity is relative, *i.e.* that the amount of infection displayed is to some extent dependent on the amount of infection to which the 'salted' adult is exposed. With increased dosage of infection the average parasite value of the community may be raised and appreciable attacks become more frequent, and the labour force may then appear to its employers to be suffering unduly from fever. The mechanism would appear, however, to be an entirely different one from the occurrence of an epidemic among a non-immune community, and the practical difference will probably lie in the fact that whilst the 'salted' population are perhaps liable in the fever season to occasional attacks of sickness, an 'unsalted' population in the same conditions would be completely incapacitated. There can be no doubt that in weighing up the advisability of action against malaria, a reasonable allowance must be made for the fact that a 'salted' labour force is not in the same urgent need of protection that a 'non-immune' one would be." The writer would emphasise the high practical value of the observations described in these few but comprehensive paragraphs.

Hypothesis regarding the mechanism by which immunity to malaria is established.—The most interesting speculation published in recent years regarding the mechanism by which immunity to malaria is developed, is that of WARRINGTON YORKE and MACFIE.[1] They state: "There is, in our opinion, a considerable mass of evidence indicating that man exhibits some degree of immunity to malaria. His natural immunity is but slight and in the vast majority of cases insufficient to prevent the development of the infection; in patients who have recovered, either spontaneously or after medication, from an acute attack of the infection the immunity may be increased to such an extent that it may be impossible to re-infect for various periods which are probably much shorter in the European than in the Native; and, finally, in cases where the symptoms have subsided spontaneously, without the complete disappearance of parasites from the blood, re-infection by the feeding of infective mosquitoes does not result in an exacerbation of fever. The immunity is, however, relatively slight, and there is evidence that the malaria parasites readily develop an immune-body resistance. It is important to note that immunity developed against one species of Plasmodium does not confer a similar protection against the other species.

"The above considerations appear to us to afford considerable support to the hypothesis that the essential factor for the production of cures in malaria is the capacity of the host to produce immune-body, in response to the antigen formation resulting from the destruction of a considerable number of parasites by a medicament. When, for any reason, the host is unable to produce immune-body in sufficient amount, sterilisation does not take place and a relapse occurs. We surmise that certain individuals are unable to produce a sufficiency of immune-body to sterilise the malaria infection owing to ill-health at the time of infection and treatment, or possibly owing to a personal idiosyncrasy, and that these are the patients who develop eventually into chronic relapse cases. The immune-body produced in such cases is insufficient to destroy all the parasites which have escaped the action of the quinine; the parasites which persist gradually acquire an immune-body resistance, so that

[1] *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XVIII, Nos. 1 and 2, March 20 and May 15, 1924, pp 24, 25.

hyperendemic conditions. I shall call it the stage of *acute infestation*. It is extraordinary to consider that a small baby should be able to pass successfully through a two-year-long attack of malignant tertian, which is what such a stage amounts to.

"In children of age 2–5, who have been resident on the estate for at least three years, the proportion infected is still as high as ever, but the average value of the infections is now altogether different, for the average number of parasites is now only 1,200 per c.mm., and the highest infection encountered one of 5,420 parasites per c.mm. For the sake of illustration we may say that at this stage the child now only has an attack about once in 25 days.

"Through age period 6–10, among those who have passed through the ordeal of acute infestation, the numerical value of infections was under 1,000 per c.mm., though the actual infection rate was still approximately 100 per cent. The period following acute infestation and lasting through childhood to adolescence we may call the stage of *immune infestation.*

"The net result of childhood passed under hyperendemic conditions is the acquirement of a form of immunity. It is probable that immunisation is produced not by infections and attacks scattered through the age of childhood, as I think has generally been supposed, but by a period of terrific parasitic infestation lasting some two years, followed by a changed state in which parasites are still to be found, but in small numbers. The period of acute infestation should normally start shortly after birth, but in the case of immigrants may commence at a later age.

"The cases in which crescents were found in the children gave an average of 6,154 parasites per c.mm. and five of the infections were over 10,000 per c.mm. Crescent formation was therefore associated with the large rather than the small infections. Twenty-two of 37 children in which crescents occurred were under two years' residence, and 13 in children of 3–6. Crescents were therefore more characteristic of the period of acute infestation.

"*Malarial infection in adults in hyperendemic areas.*—Taken collectively the percentage infected among adults was 49, and the average parasite value 122. The number of infections over 5,000 per c.mm. was *nil*, and there were only five infections of 1,000 per c.mm. or over. Only one infection (4,040) approached what we have previously taken as 'attack' conditions, and we may say that at this time of the year an adult, on the average, would seem to have an attack only about once in 158 days (five months). *This peculiar relationship of low value of infection and high percentage infected must represent immunity in the adult.* A European living without protection, as most of these men do, in the midst of infection would undoubtedly suffer much more severely.

"Considering the history of malarial infection among those living in this hyperendemic area, from birth to adult life, the following sequence is observable.

Stage.	Age and residence in years.	Spleen rate.	Per cent. infected.	Average parasites.	Frequency of attack
Acute infection .	1–2	75	100	12,620	Almost continuous.
Immune infestation .	3–5	88	96	1,320	Once in 25 days.
" " .	6–12	71	86	1,018	Once a month.
" " .	12–16	46	50	198	Once in 3 months.
" " .	Adult	11	50	122	Once in 6 months.

. . . .

"We may epitomise the conclusions in this section by saying that under

The great epidemics of malaria in India have been associated with one of many circumstances, such as overflowing of rivers, heavy rainy seasons, expansions of irrigation works, famine relief works, unusual activity in railway extension and industrial expansion generally. Except in the first two, there is invariably gathered together a large amount of coolie labour. "Labour aggregation with all its attendant conditions appears, in this province (Bengal) at least, to supply the key to the riddle of epidemic malaria, in which it seems to have played a part far more important than movement of populations or general scarcity and want" (CHRISTOPHERS and BENTLEY.)[1]

Anyone who has seen a big canal irrigation work, or a railway embankment in process of construction, can comprehend what is meant. Here we have large numbers of people, poverty-stricken and with lowered physiological resistance, working hard, many harbouring malarial gametocytes. They are unprotected by mosquito nets or otherwise, often three parts naked, and crowded into huts giving free access to anophelines. The new excavations created as work progresses rapidly multiply the number of anophelines, and so the diffusion of malarial fevers occurs with almost geometrical progression. In this way areas which were known to be only slightly malarious have been converted into virulent malarious centres. Here is an accumulation of circumstances which is largely responsible for the intensity attained by malaria wherever the undertaking of large projects in a malarious district involves the employment of numerous labourers and the establishment of labour camps. We find the malarial incidence very high and the virulence of the infection unusually great, a condition in constant operation in various parts of India. From these virulently malarial camps malaria is disseminated in all directions when the victims return to their homes sick, deserting or dismissed, only to be replaced by others in whom the process is repeated. It is in the crowds of these camps that a considerable amount of residual malaria continues, to maintain malaria during the non-malarious season, and from them the newly born anophelines of the monsoons begin diffusing malarial infection wholesale.

Effects of famine relief works.—Famines are specially prone to effect a devastation of the population through malarial diseases, for the impoverished physiological condition of the people permits of malaria parasites producing their worst effects, and this occurs at a time when, as a rule, little can be done to keep malarial infection in check. Moreover, the large collections of coolies that occur in all famine relief works are particularly fruitful in effecting a dissemination and intensification of malaria by reason of a high degree of susceptibility to infection.

Effects of railway construction.—The construction of railways in India has largely helped to maintain and disseminate malaria, and some districts previously only mildly malarious have been rendered severely so by railway works. This is not exceptional to India; it has had the same effect in all countries where malaria is endemic. The construction of railways operates in two ways—by the formation of borrow-pits which are favourite breeding places of anophelines, and by the embankments which tend to intercept the flow of surface water which would naturally flow into lower lands and find its way to natural water-courses. Rain falling on to the embankment and draining into the borrow-pits helps to keep these latter charged with water. A local rise in subsoil water must be expected from the action of these factors. Railways in India were, of course, started long before we understood how malaria was disseminated by anophelines, but not before we knew that all engineering works interfering with subsoil water drainage gave rise to increased unhealthiness.

[1] *Proceedings Indian Medical Congress, Bombay*, 1909, p. 81 *et seq.*

the relapse strain, although reacting to quinine as usual, is not completely destroyed by immune-body. In this connexion it is interesting to note that among the three or four relapse cases of our mosquito-infected series which have been observed sufficiently long, two have already relapsed a second time, as also has one (quartan) of the three cases which have relapsed among our inoculated patients." (See also pp. 214, 215.)

To sum up, then, an important part in the development is played by the vague forces which may be characterised as the *natural resistance of the individual*; that is, his ability to develop some unknown form of immunising body through reaction of his economy. This natural form of protection is fostered by a wholesome, generous and nutritious diet, comfortable housing and clothing, and freedom from debilitating conditions.

That there are other peculiarities in the reactions of different individuals to malarial infection is shown by the fact that in a group of 68 cases of induced benign tertian malaria the character of the initial fever in 36 was continued remittent, in 12 frankly intermittent, and in 20 irregular.

It is certainly the case that locality has much to do with reduction of relapses in benign tertian, in some places no form of treatment appears to eradicate the infection within a reasonable time (say a few months), in other places no such difficulty is experienced. Prof. J. W. W. Stephens, in a note to the writer, states: "During the war, while unable to cure simple tertian infection in Liverpool, I was astonished to find that at Bangour, near Edinburgh, they were not troubled by the incessant relapses that occurred elsewhere. I put it down to fresh food and a splendid climate."

Congenital immunity does not exist.—The Indian does not transmit any of his partially acquired immunity to his offspring. This is curious, because the people of India have never been free from malaria for thousands of years, and it might be thought that in, say, fifty generations or so some sort of specific resistance would be acquired. The *prima facie* inference is that the production of a permanent immunity by artificial means is not very hopeful, although it is possible that some day we may discover a means of bringing about a reliable temporary immunity.

G.—RÔLE OF MAN IN THE DISTRIBUTION OF MALARIA IN INDIA

Effects of aggregation of large gangs of labourers employed on engineering works.—This section deals with the manner in which human agency is largely responsible for the distribution of malaria in India. The rôle of man here is one of paramount importance in the endemiology, epidemiology and prevention of malaria in India. The rapid expansion of traffic and facilities for travel by rail have their influence, but the chief factors are other than these.

In the production of malarial fevers in man three agencies are necessary—susceptible human beings, certain species of anophelines, and malaria parasites. In endemic malarial places these three are as a rule abundantly present during the malarial season, and in general terms it may be said that the intensity of the endemicity varies with the relative quantity of these co-existing agencies. It is easy to quote instances in which there are comparatively few malaria-carrying anophelines with a moderately severe endemicity, *e.g.* in localities where there is a large number of susceptible persons; or places where there are numerous malaria-bearing anophelines with a low endemic malarial index, *e.g.* where there are few susceptible persons; but these instances do not affect the general rule stated.

pits " (excavations formed by removing earth for raising the level of the roads above the surrounding areas), and, when finished, the roads interfere with the proper surface drainage and raise the subsoil water level.

These excavations become veritable nurseries for mosquitoes, the first fall of rain filling them; they become reservoirs of stagnant water that fill with wild grasses, weeds and vegetation generally, which give cover to larvæ and permit of their multiplication without hindrance. These are amongst the most frequented breeding grounds of anophelines. All houses or huts within the radius of flight of anophelines from the roads may therefore be invaded by malaria-carrying mosquitoes. Borrow-pits from road-making form one of the main sources of malaria-carrying anophelines throughout India, and they can be legitimately incriminated in the production of a vast amount of malaria. This has gone on for generations. In all villages along such roads there are never wanting cases of malarial infection to perpetuate the different species of malarial organisms. The process of dissemination requires no description.

One would here inveigh as forcibly as words can express against the wantonness of such indiscriminate disruption of the soil level in road-making. It should be rendered an illegal proceeding. It should be legislated on as strictly as was done in the whole of the Panama Canal Zone with such successful results.

When roads in India interfere with land drainage they necessarily raise the level of ground water, and as a result increase the breeding of mosquitoes, and, through the latter, increase the prevalence of malaria. Borrow-pits near human habitations may be injurious to public health and, in India, a source of malaria through Anopheles.

There is scarcely a village in the whole of India that is not surrounded by its borrow-pits; in most of them such pits are to be found scarring the interior of the village also. These have been created by the villagers themselves in excavating the soil for making mud walls or sun-dried bricks for building purposes.

The manner in which malaria may be considerably reduced amongst gangs of labourers is dealt with in PART III, pp. 382–384.

Effects of excavation of the soil; production of hyperendemicity.— —Opening of the soil is often observed to be associated with malaria. Formerly this was ascribed to miasmata or emanations from the earth. Now we know that this increase is at any rate partly due to excavations creating breeding grounds for anophelines and consequent malaria, and to the effects of heavy work on ill-fed labourers exposed to all weathers, many of them already infected, and all herded together—the conditions which S. R. CHRISTOPHERS has aptly grouped under the name *Malaria of tropical aggregation of labour*. These conditions may not be of a temporary nature; when they exist on an extensive scale they may affect wide areas of country and are liable to be associated with malaria of a severe type. They form one of the great widespread causes of malaria in India, one which is always in operation in several parts of the country at the same time.

Effects of non-immune immigration.—The immigration of a large body of non-immune people into an endemic area is, next to anophelism, the most important factor in bringing about epidemics of severe malaria in India; the condition brought into existence has been named *hyperendemicity* by CHRISTOPHERS and BENTLEY.[1] A susceptible community is required to spread malaria. The constant flow of susceptible new-comers to an endemic area is important

[1] "The Human Factor in Malaria," *Proceedings Indian Medical Congress, Bombay*, 1909, p 81.

One of the most important points in connexion with railway construction is the filling up or draining of all borrow-pits. The task is prodigious, but it is of importance that it should be carried out. The drainage could be effected readily by a general levelling of the pits and a rough canalisation of areas between them effecting a drainage of accumulated waters to lower levels. The amount of coolie labour always available in the permanent-way establishment of railways should make this a relatively inexpensive operation.

The third factor in operation while railways are under construction is the aggregation of labourers, many already infected with malaria. Its influence has just been considered. As there are many thousands of people constantly so employed in India, and as such employment has gone on for the last fifty years, the influence of this factor in the perpetuation of malaria in India is considerable. It should be a fundamental hygienic principle in the construction of all new railways in India that three important factors—creation of borrow-pits, raising the level of subsoil water, and elimination of cases of malarial infection from amongst coolie labourers—be kept fully in mind, if not actually legislated for. Nothing should be done which can render the tract malarious. This is readily carried out by a little forethought and some initial extra labour.

Effects of irrigation canal works.—In the construction of irrigation canals we have in addition to the susceptible labourers, who are employed on the main work and its various channels, village populations, and so we get malarial infection disseminated throughout the district, in which the maintenance of malaria parasites is permanently secured by the vast number of breeding grounds created for anophelines through raising of the subsoil water level, and consequent formation of pools of water in the whole of the irrigated area.

At one period (1906) the writer followed the course of a severe outbreak of malaria in 1,950 families on canal work which consisted of clearing the bed of stones and alluvium carried down with the current and deposited. He was able to trace the various external factors that were in continuous operation in maintaining the hyperendemicity and in spreading malaria from this centre of aggregated labour to other places.

The writer was at the time encamped with his regiment at Madhopur (Punjab) during a malarious season; that station forms the head of the Bari Doab irrigation works; every house and hut was full of malaria-carrying anophelines. These canals irrigate the fields connected with villages for many square miles; the water in the fields around villages was bubbling to the surface in hundreds of places; there was no provision for drainage of the subsoil. In such an instance as this no malariologist would recommend that any radical efforts to exterminate mosquitoes be made. Isolation of infected persons, and quinine treatment of the infected have alone to be relied on. Mosquito nets and screening are out of the question with these labourers (see p. 383). In such cases there are not only numerous breeding pools from seepage, land springs, etc., but new ones are cropping up continually in unexpected places.

Effects of road-making.—Collections of coolies in connexion with road construction operate in distributing malaria in the same way as does the making of railway embankments, although to a less extent, as the size of the camps is smaller. The making of roads affects malaria in other ways, which it is convenient to consider here. Road-making is a prolific source of breeding grounds for mosquitoes. This is especially so in extensive roads on the flat country along the larger rivers (Ganges, Jumna, Brahmaputra, etc.) and along the sea coast. They create these breeding spots by the formation of "borrow-

This type of malaria is more or less confined to certain tracts, especially in North-West India. In the dry, almost desert conditions of the Western Punjab, with a scanty rainfall, epidemic malaria has never occurred. Yet epidemic malaria occasionally attacks the dry province of Sind. Epidemic malaria has never occurred when the monsoon rainfall has been deficient; most of the epidemic years have been years of heavy rainfall. Nevertheless, the heaviest rainfall may not be associated with epidemic malaria, or may be linked with a small and local epidemic only.

The mortality in the affected areas during these epidemics is appalling. In the 1908 Punjab epidemic the monthly mortality of the Punjab, which is normally 50,000, in October and November was 307,316; the weekly mortality rose in some towns to 420, reaching 493, per 1,000 per annum. The most striking features of the epidemic were its simultaneous appearance over all the area affected (many thousands of square miles), its extraordinary severity and the conspicuously high infant mortality. Although the whole Punjab suffered there were foci of special severity, particularly the districts of Gujrat and Gurgaon, the latter running into the United Provinces.

There have been seven or eight of these epidemics recorded. Each has affected different areas, except that the Gurgaon district was also the focus of the 1879 epidemic. Particular towns, even large towns, are attacked. Amritsar has been twice decimated by epidemic malaria. "It is this epidemic form of the disease which in the Punjab is in every way the most important manifestation of malaria."[1]

The history of epidemic malaria has shown that irrigation canals have had very little to do with it. Irrigation is concerned with endemicity, and even hyperendemicity, but has little influence on the widespread outbreaks under discussion. Economic stress, too, has usually little influence on epidemic malaria, except when the latter extends to a district poorly provided with crop water, and in which the previous year's monsoon was very defective.

It is now possible to forecast with some degree of accuracy the extent, if any, to which epidemic malaria will occur in the Punjab in the autumn. The forecast is based upon the rainfall of July and August with a view to estimating the malarial incidence in October and November. The forecast is usually completed by September 15. This has been done by GILL for the last four years with such nearness to fact that the hypothesis upon which the method of forecasting is based is something more substantial than a mere epidemiological speculation.

During these epidemics the infections are more virulent than usual, and the ratio of malignant tertian cases much higher. The victims must repeatedly receive exceptionally large doses of sporozoites, giving rise to intense infections (as measured by the number of parasites in the peripheral blood) and to frequent relapses, not easy to prevent if the infection has not been vigorously treated by quinine in the early stages. In epidemic seasons there are vastly more malaria cases among the people who are receiving no quinine treatment, and are therefore disseminators of the disease, than are actually in hospitals.

So far we only partly comprehend the mechanisms by which epidemics of malaria are brought into existence. Some elaborate theories have been formulated to account for them. The most obvious point so far brought out is that these fluctuations depend upon the distribution of Anopheles: these insects from time to time, under propitious conditions, increase vastly in numbers and extend from their usual habitat over wide tracts.

In epidemic malaria in India there is no new parasite; only the ordinary

[1] S. R. CHRISTOPHERS, "Report on the Punjab Malaria Epidemic of 1908," in *Paludism*, No. 2, January, 1911, p. 19.

endemiologically. In the permanent inhabitants the malaria rate remains the same. When the number of susceptible immigrants is small the acquired immunity of the permanent inhabitants is sufficient to protect them from any aggravation of malarial intensity, but when large and fresh lots are constantly arriving, the previously relatively immune indigenous inhabitants now become widely infected—their previous immunity is no longer able to protect them against the larger number of sporozoites introduced by anophelines. A malarious area into which there is a constant flow of non-immune immigrants has its malaria maintained, increased and sometimes intensified, and in some years this may be a noteworthy factor in the production and spread of epidemic malaria from such centres. In making malaria surveys we repeatedly come across small localised outbreaks of malaria that have been started by the arrival of groups of infected people on the one hand or non-immunes on the other. Lt.-Col. S. R. CHRISTOPHERS[1] also remarks that in endemic malarious localities the constant immigration of susceptible persons is one of the main sources whereby the disease is kept up. When such importation of susceptible persons is maintained in these places, every one becomes infected in a short time, even when the number of anophelines is very small, assuming that there are at least some malaria-bearing anophelines.

Transportation of infected anophelines and human carriers.—A common way of acquiring infection is by halting and sleeping on board *country boats* in the neighbourhood of river-side villages or towns. A large amount of the traffic of India is carried out in such boats, and a great deal of floating malaria exists. *River steamers* are also sources of malaria. The crews and passengers in the latter, and boatmen and labourers in the former, are infected. This form of infection may to some extent be avoided by anchoring or tying up steamers in the middle of the stream, and in boats by tying up at some distance above or below a village. A great deal of the malaria of India, Assam and Burma—along the basins of the Ganges, Brahmaputra and Irrawaddy—is acquired in this way. The third-class waiting rooms of railways, which usually consist of open sheds or iron-barred enclosures, with a roof, are universal sources of malarial infection and its dispersion in all directions.

H.—EPIDEMIC AND INCIDENTAL MALARIA IN INDIA

Epidemic malaria.—There are periodical fluctuations in the intensity of ordinary endemic malaria in India. After years of normal and comparatively slight malaria the disease not only becomes severer in its endemic areas, but spreads and becomes an epidemic. Epidemic malaria is a strange phenomenon. It occurs irregularly, descending with decimating influence, after some years' interval, on large tracts, not only those with high endemic incidence, but places that are little if at all affected in normal times.

In the Punjab, North-West Frontier Province, and parts of the United Provinces vast autumnal epidemics of malaria occur periodically after a number of successive years of ordinary endemic malaria. The areas involved can be plotted out by the increased number of registered deaths and are *focal*, that is, they are greatest at the centre of the epidemic area and fade towards the periphery.[2] These periodical epidemics affect urban as well as rural areas. The terrible malaria epidemic of 1908 in the Punjab had two foci, and affected an area of about 50,000 square miles.

[1] BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. II, pp. 1552, 1553.

[2] S. R. CHRISTOPHERS, "Report on the Punjab Malaria Epidemic of 1908," in *Paludism*, No. 2, January, 1911, pp. 17 *et seq.*

he may have them at some future time; and still others think of malaria-carriers as infected persons without clinical symptoms of malaria. "Any person who has any malaria parasites in him, whether in the bone marrow, spleen or circulating blood—however small the number—may later have much larger numbers in the circulating blood. The influences which control the multiplication of malaria parasites within the body are not definitely known. Neither do we understand those influences which control the production and the longevity of gametocytes, and their appearance in the circulating blood. Nor are we able to predict the course of events in this regard in any particular case. Given a person with the smallest possible number of parasites, perhaps all lodged in the bone marrow and the spleen, and none to be found in the circulation, there are a great number of possibilities. The parasites may die and the infection disappear. After a variable period the parasites may multiply until they are sufficiently numerous to be found in the peripheral circulation, and possibly to cause clinical symptoms. The parasites that appear in the circulating blood may be asexual parasites only. Both schizonts and gametocytes may appear in the peripheral blood, in which case the blood may be infectious for anophelines. The number of gametocytes present may, or may not, be sufficiently large for there to be any reasonable chance for anophelines that may feed on the carrier to become infected. The gametocytes may, or may not, be able to infect anophelines, because of some unfavourable condition or quality of the blood or of the parasites. The gametocytes may be sufficiently numerous, and conditions may be sufficiently favourable, to cause infection of part or all of the anophelines that feed on the carrier."[1]

We do know definitely that only persons who at the time have fully developed gametocytes in the peripheral blood are able to infect anophelines with human malaria parasites. But a person who has no gametocytes in the peripheral blood to-day, whether he has asexual forms or not, may a week later have large numbers there. Therefore every infected person is a potential source of infection to others, whether his infection at the time conforms to one or another of the several possibilities given above—"a non-effective carrier may become an effective carrier at any time, or *vice versa*."[2]

As man (we assume) is the sole malaria-carrier, and since all potential carriers may become effective carriers at any time, any reduction in their total number in a given inhabited place will correspondingly reduce the local dissemination of malaria. If, say, 50 per cent. are eliminated the prevalence of malaria is *pro tanto* lessened. Hence every anti-malarial campaign should aim *inter alia* at the effective cure of infected persons. This brings us to the main point of this section—that of directing attention to the necessity of effective treatment of malaria cases during the acute stage, that is, during the early paroxysms, and *subsequently*. If every malaria case treated by medical men were really cured there would be a material reduction in the number of malaria-carriers in the country—the writer would aim at eradicating the infection in every such case. We shall see later on that, in certain limited circumstances, it may be possible to sterilise the malaria-carriers responsible for transmission of the disease. In the malarial season the writer has found gametocytes in 5 to 33 per cent. of "healthy" native children up to ten years of age, and in 0·5 to 3·5 per cent. of adults. Of soldiers going about their ordinary duties in the Macedonian Campaign, the percentage of malaria-carriers sometimes reached 25; 70 per cent. of the mosquitoes invading the tents

[1] C. C. Bass, "The Relation of the Malaria-Carrier to Malaria Prevalence," in *International Conference on Health Problems in Tropical America*, 1924, p. 61.
[2] *Ibid.*, p. 63.

parasites found at all times are present. Presumably the vast number of these introduced, and the large quantities of malarial toxins they manufacture, stamp epidemic malaria with its virulence, while the victims are infected several times every day, and one infection is superimposed on another in rapid succession.

Lt.-Col. A. C. Gill, I.M.S., who has had much practical experience of epidemic malaria in the Punjab, considers these periodical outbursts to be due to imperfect immunisation of the population owing to the intermittency with which severe malarial conditions arise, the real determining or exciting cause of these being flooding, which excites anophelism.

It has been suggested that anophelines possess the migratory instinct, and that, like caterpillars, they proceed in vast numbers, spreading from one district to another in search of water. The writer does not know whether this point has been investigated as a possible explanation of the *epidemic* malaria that occurs in Northern India.

The facts then suggest that, although much valuable information has been collected about epidemic malaria by highly skilled malaria experts, there are still gaps in our knowledge regarding its causation, and that for the present it is necessary to be cautious in assigning it to any particular cause or causes (see Appendix I).

Incidental malaria.—This is the term applied to the malaria which affects European and other immigrants to an endemic area, where the indigenous inhabitants, although the cause of the trouble, appear themselves to suffer little from the effects of the disease. British troops fresh from England, during the malarial season, may be taken as types. People passing through endemic areas, putting up in the village *zayat*, caravansary or rest-house (usually a large hut or an enclosed space surrounded by cubicles), or the local *dâk* bungalow, acquire malaria similarly. Troops marching through such areas, unless camped or bivouacked well away from the local population, are similarly liable to infection. The same occurs in campaigns in malarious countries.

I.—THE HUMAN "MALARIA-CARRIER"

Importance of the human "malaria-carrier."—This is emphasised in several parts of this volume. The object of this section is to concentrate attention on him, and inquire to what extent he may be eliminated as a communicator of malaria. He is one of the two great dominating and controlling factors in the dissemination of malaria. So far as we know, man is the only intermediate host of the parasites. Inoculation experiments with infected anophelines have failed to infect all other animals; and the same negative results have followed the injection of human malarial blood into animals. No other animal is known to carry human malaria parasites naturally. The possibility has never been lost sight of, and if any of them did so, the fact could hardly have escaped discovery.[1] It may be that the whole of this field has not yet been explored, and we must still admit that there is a remote chance that there may be some other animal carrier.

The term *malaria-carrier* does not convey the same meaning to everyone. Some think of the carrier as one with fully matured gametocytes in his peripheral circulation, and therefore, presumably, capable of infecting anophelines; others consider that a person having malaria parasites of any kind in the blood is a carrier. Others, again, define a carrier as one with latent infection but not necessarily with any parasites discoverable in his blood at the moment, although

[1] C. C. Bass, "Studies on Inoculation of Experimental Animals with Malaria," *Am. Jl. of Trop. Med.*, ii, 1922, p. 107; and *International Conference on Health Problems in Tropical America*, 1924, p. 61 *et seq.*

most satisfactory method of prevention would be for the soldiers to camp out in tents during that season on a site where they would be at a safe distance from the dangerous zone; this applies to many military cantonments, especially where the quarters of the civil community dovetail into those of the troops, and where exceptionally large numbers of native children live near the barracks. There are, of course, other means of dealing with this local problem—shutting off the water from the irrigation channels for several hours twice a week during the anopheline breeding season, screening the barracks and hospital, treating all

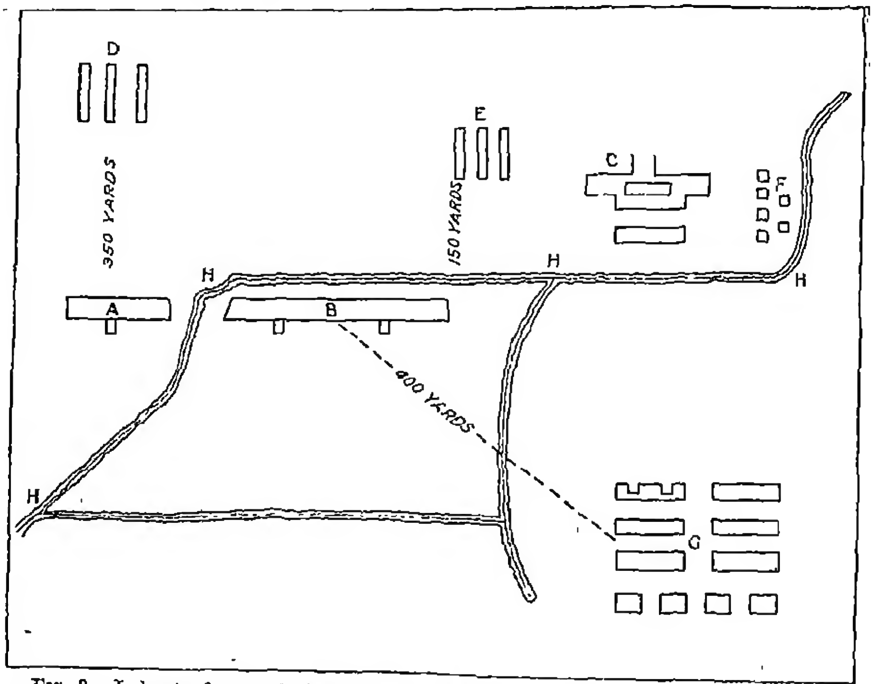


FIG. 3.—Indicates how malaria is spread to troops in military cantonments by infected Indian children.

From Lt.-Col. S. P. JAMES's *Malaria at Home and Abroad.*

A and B. Barracks of European troops.
C. Hospital and military prison.
D and E. Native followers' quarters, containing perhaps 200 native children, from 40 to 60 per cent. of whom had malaria parasites in their blood.
F. Hospital followers' quarters, containing 40 or 50 children, 60 per cent. of whom had malaria parasites in their blood.
G. Regimental bazaar, containing numerous children, most of them infected.
H H H H. Irrigation channels.

infected native children with cinchona febrifuge, and so forth. Figs. 45, p. 132, and 46, p. 134, also demonstrate two other instances of the way in which the human carrier and the anopheline carrier are in close association, and how the disease is disseminated. During the malarious season, that is, while anopheline malaria vectors are operating on man, there are always throughout India a certain number of healthy human malaria-carriers going about their ordinary avocations disseminating malaria through anophelines. This is a very serious, important and incontrovertible fact.

occupied by this 25 per cent. were in certain instances found gorged with blood. The ease with which all occupants of the tents soon became infected is readily understood.[1] The importance of the habitation in the dissemination of malaria cannot be over-emphasised.

The malaria-carrier is a much more important person in a community than the actual case that comes to the hospital or outdoor dispensary. It bears insistence that, if we treat symptoms alone—that is the paroxysms—we do not cure the infection; if we stop treatment when the paroxysms cease, we do so at a time when the patient is about to become a dangerous malaria-carrier. Malaria is not, like the infectious fevers, self-limiting as to duration; if not properly treated by quinine it may go on indefinitely. The most important way in which the practising physician can help in solving the malaria problem in India is to bring about a complete eradication of the infection in every case of malaria that comes under his care for treatment. Practically any one of the STANDARD QUININE TREATMENTS given in PART III (pp. 272–276) will ordinarily effect a cure if properly carried out. These facts should be thoroughly engrafted into the mind of every medical student.

The tolerance of infection without manifest symptoms, so characteristic of the malaria-carrier, signifies, not immunity, but some neutralising influence against the pathogenic effects of malarial toxins. Real immunity signifies parasite-proofness, the absence of infestation in the individual in the presence of the ordinary agencies for bringing about infection. One of the aims of malaria workers in the future may be to establish such immunity in man. The brothers Sergent worked out that the normal immunity rate against Proteosoma in canaries is 0·76 per cent., which can be increased to 21 per cent. by injecting blood taken from a canary during the inoculation period after an experimental infection, and to about 80 per cent. by the injection of sporozoites which have been kept *in vitro* for twelve to forty-eight hours. These experiments are highly suggestive of one line of investigation for the working out of immunity to malaria parasites in man.

The length of time an untreated person may be a malaria-carrier in India is important in prevention. Yellow fever has been eradicated from most of its wonted haunts mainly because yellow-fever patients are infectious for three days only. Malaria cases may carry parasites for years.

During an examination of 31,000 persons in Bolivar County (U.S.A.) C. C. BASS found that 10 per cent. of those who denied present or recent clinical evidence of malaria were infected. WENYON found in Macedonia (1915–19) that, in 8,000 men who had had symptoms of malaria, 25 per cent. were carriers. CHRISTOPHERS and SHORTT gave corresponding facts regarding malaria in Lower Mesopotamia.

Fig. 3, p. 54, shows how malaria is disseminated and maintained in many military cantonments in India, the main human carriers being infected Indian children. The native children concerned formed a constant and abundant source from which the numerous Anopheles which bred in the irrigation water-courses became infected. It will be obvious that in these conditions the men in the barracks must suffer severely from malaria; they were in the midst of an area of infected Anopheles, and unless very stringent precautions to guard against mosquito bites were taken, it could only be by a fortunate chance that any man escaped the disease. In the locality from which this example is taken the season of new infections lasts only three months, and no explanation is necessary to make it plain that in the particular instance cited the simplest, cheapest and

[1] C. M. WENYON, *Malaria in Macedonia*, 1915–19, pp. 6, 7 and 43.

the two hosts. Anophelines biting patients in whom only the schizogonic phase of the parasite is in progress, are not capable of transmitting malaria—all the young, intermediate and sporulating forms are disintegrated and digested in the stomach and intestine of the mosquito.

In malarious places during the endemic season there are malarial cases, and a number of malaria-carrying anophelines in whose salivary glands sporozoites are to be found. The experiment of transporting malaria-infected anophelines from endemic malarial foci to non-malarious places, and inoculating and infecting people who have never been out of these non-malarious places, has more than once been carried out successfully.

A non-malarious region, having certain species of anophelines, remains such so long as there is an absence of malaria-infected human beings. With the accession of the latter a healthy place may become malarious. A mildly malarious region contiguous to a very malarious one may, during epidemic malaria in the latter, become severely malarious by the gradual extension of the habitat of malaria-infected anophelines. This occurs during periods of severe epidemic malaria in India.

The recession of malaria in countries formerly infested, but still possessing numerous Anopheles capable of carrying malaria, deserves the closest attention. It is doubtful if any one factor explains this; it is probably due to a combination of such factors as drainage, sound agriculture, better housing and sanitation generally, and *reduction* of malaria-carrying Anopheles. Potential anopheline vectors are not alone sufficient for the spread of malaria; they exist in many places where there is no malaria. Where anophelines exist they can only transmit malaria when the average temperature is not below 15° to 16° C. If it fall below this they may get infected and produce zygotes, but no further development of malaria parasites takes place. Conversely, imported human malaria-carriers do not cause the spread of the disease if anopheline vectors are not present.

If infected anophelines are kept from biting healthy persons malaria does not occur in the latter. In 1900 Drs. Low, Sambon and Rees, of the London School of Tropical Medicine, had constructed in Ostia, one of the most malarious portions of the swamp land of the Roman Campagna, a small house that was thoroughly protected by mosquito-proof wire-gauze doors and windows. The house was, during the malarious season and the breeding time of anophelines, occupied by a number of people whose movements were not restricted, except that they entered the house every evening at sundown and remained inside till daylight. The night air was admitted freely, and during the rainy season the experimenters purposely got repeated soakings in the rain. They did not take quinine prophylactically. None contracted malaria, whilst their neighbours, who were not protected from mosquitoes, suffered severely. Moreover, there was yet another undesigned and striking control. A considerable patrol of police, sent from Rome to arrest a murderer, spent a single night near the experimental house and forthwith returned to Rome. About a fortnight later all went down with malaria. The British Red Cross Greek Refugee Mission in 1923 practically repeated this experiment. Maj.-Gen. Sir James Stewart, the Rev. R. H. Cragg and the author lived in the Red Cross train for several months in Macedonia and Western Thrace, where malaria of a severe type was very prevalent. The only anti-malarial precaution adopted was to have all doors and windows of the train thoroughly screened against mosquitoes, and only one door of exit and entrance. None of the party contracted malaria except the cook and his mate, who on account of the heat at night insisted on sleeping outside in the open in the immediate vicinity of the Red Cross coaches.

J.—INDIAN ANOPHELINI AND THEIR HABITS

It is proposed to deal with the subject of Indian Anophelini under the following headings:

(i) RELATION OF ANOPHELINI TO HUMAN MALARIA (by way of an Introduction); (ii) CLASSIFICATION OF MOSQUITOES; (iii) GENERAL CHARACTERS OF MOSQUITOES; (iv) COLLECTION, MOUNTING AND EXAMINATION OF ADULT MOSQUITOES; (v) EXTERNAL ANATOMY OF MOSQUITOES; (vi) INTERNAL ANATOMY OF MOSQUITOES; (vii) OVA OF MOSQUITOES; (viii) LARVÆ OF MOSQUITOES; (ix) RECOGNITION OF SPECIES OF ANOPHELES; (x) NOMENCLATURE OF INDIAN ANOPHELINI; (xi) SYNOPTICAL TABLE OF INDIAN SPECIES OF ANOPHELINI; (xii) GENERAL REMARKS ON MALARIA-CARRYING ANOPHELES OF INDIA; (xiii) DESCRIPTION OF MALARIA-CARRYING ANOPHELES OF INDIA; (xiv) STUDY OF AVIAN MALARIA; CULEX FATIGANS AND PROTEOSOMA IN SPARROWS; (xv) BIONOMICS OF MOSQUITOES IN INDIA; (xvi) STUDY OF MALARIA PARASITES IN INFECTED ANOPHELES.

(i) RELATION OF ANOPHELINI TO HUMAN MALARIA

Introductory remarks.—Many theories of malaria have been built up, exploded and abandoned in the past, but the modern view concerning its causation is indestructible, simple and almost complete. It is obvious that until the manner in which malarial infection was brought about in human beings was known, it was not possible to formulate any rational basis for the general prevention of malaria. An enormous amount of work was done after the discovery of malaria parasites in human blood with a view to elucidating this highly important question, and this work has resulted in a solution of the problem by a complete demonstration of the relationship of the anopheline cycle to malaria parasites. The views held anterior to the discovery of this relationship were chiefly connected with the conveyance of malaria to man through air and water. We need not deal further with these obsolete opinions.

That malaria may be transmitted to man by insects is no modern conception, for VARRO, COLUMELLA and other writers of ancient Rome suggested that malarial fevers might be disseminated in this way. LANCISI (1717) mentions the mosquito as a possible transmitter of malaria. A. F. A. KING, of Washington, advanced this view in 1882. The idea that mosquitoes are instrumental in disseminating malarial fevers has been for centuries entertained by the inhabitants of several countries. The Cingalese have long associated malaria with mosquitoes; in certain parts of Italy the peasants have for many generations believed that malarial fever is produced by these insects; the natives of the highlands of Kenya Colony declare that, when they visit the unhealthy lowlands, they are bitten by an insect they call *Mbu* (mosquito); they get fever which they also call *Mbu*. LAVERAN, KOCH and PFEIFFER, before the problem had been worked out, suggested that the mosquito might be a malaria-carrier (see PART I, SHORT HISTORY OF MALARIA, pp. 1 *et seq.*).

The mosquito-malaria theorem[1] explains almost all the epidemiological and endemiological phenomena connected with malarial fevers—the period of incubation in the mosquito and the subsequent period of incubation in man. At no period of their life-history are the Plasmodia of malaria found apart from

[1] The word *theorem* in connexion with the relation of anophelines to malaria is used in its mathematical sense, as expressing not a hypothesis or speculation, but a *datum*, established fact, or recognised truth.

(4) *Susceptibility of the anopheline and of the individual bitten to malarial infection.*[1]

In the absence of any one of these conditions an outbreak of malaria is, as far as we know at present, impossible. Together they form the chain of the malaria cycle; if any link in that chain is broken the disease ceases. There are many places where anophelines exist without malaria; others in which there is no malaria at particular seasons, because at these seasons the conditions are unfavourable to the development of the mature forms of the parasite, or the mosquitoes do not bite.

Malaria is not acquired in uninhabited places. There is no spontaneous generation of malaria anywhere. The factors enumerated must be present whenever it is met with. Accepting these views as to the nature of malarial infection, we also recognise that there must always be a period of incubation in malarial fevers after the bite of infected mosquitoes, just as we know there is in yellow fever after the bite of the infected *Aedes* (Stegomyia) *fasciata*, and in sleeping sickness after the introduction of *Trypanosoma gambiense* by *Glossina palpalis.*

(ii) CLASSIFICATION OF MOSQUITOES

Bases of classification of mosquitoes.—There have been several bases suggested for classification in the past, but it has been found that some of these were of quite secondary importance; the result was that in many instances minor groups acquired undue importance and much confusion arose.

In the early days of mosquito investigation, and when there were only three genera, the classification was based on the characters of the palpi. It was subsequently found, when many fresh genera were created, that palpal characters were insufficient for a general classification, although useful in distinguishing species. Later the nature and arrangement of the different kinds of scales were used as a foundation for classification. In recent years an intimate study of the male genitalia and of the larvæ of mosquitoes has had much to do with the classification of the true mosquitoes.

Number of known species of mosquitoes and of Anopheles.—About 1,000 mosquitoes have been classified and described; they occur in all parts of the world. Comparatively few are connected with disease. The vast majority are wild or sylvan mosquitoes, and, as would be expected, their habits are not so well known as those of the domestic kinds. Up to the present, of the genus Anopheles 124 valid species are listed, and 42 varieties of more or less probable geographical significance, omitting 9 specific and varietal names not identified. This list includes 40 or perhaps 41 species in India and Burma. The following remarks about the Anophelini are limited to what is essential in carrying out malaria investigations in India. Those anxious to get a more complete knowledge of the adult Anopheles of India are advised to study the unique type collection in the Central Malaria Bureau at Kasauli, which has been made with infinite trouble, care and skill by the staff of the Central Malaria Committee during the last twenty years.

Metamorphosis of mosquitoes.—The mosquito passes through three very definite stages—egg, larva, pupa—before becoming an imago or adult.

What are mosquitoes ?—Mosquitoes (included in the Nematocera, a sub-order of Diptera) are small, two-winged, delicately made, long-legged insects with a long, slender proboscis and a dense covering of different-shaped scales (p. 70) on part at least of the body. All known species are aquatic in their early stage, and are active as larva and pupa. Adult females of most

[1] THAYER in ALLBUTT and ROLLESTON'S *System of Medicine*, Vol. II, Part II, p. 243.

So far only ten[1] species of Anopheles are found to be carriers of malaria in India. Of the other indigenous anophelines it is probable that certain will in the future be found to be malaria-carriers, and that others will be proved exempt. It is possible that some of these latter have, by centuries of repeated infection, worked out for themselves a complete racial immunity to the sporogonic cycle of the Plasmodia of malaria.

It is possible also that there are in malaria-carrying anophelines varying degrees of susceptibility to infection by the sexual forms of malaria parasites. We may now state that the main facts connected with the endemiology and epidemiology of malarial fevers are explained satisfactorily by the dissemination of malarial infection through anophelines. No proof is yet to hand that malarial fevers are produced in any other way. The cases cited of people acquiring malarial fever the day they arrive in a reputedly malarious place cannot bear scientific examination; in such instances it is possible that malarial infection was due to previous mosquito bites of which the patient was unconscious, or that they were relapses, or that these cases were some other form of fever. From the foregoing considerations it is seen that the distribution, spread and intensity of malaria are to a large extent governed by the conditions favourable to the occurrence of numerous anopheline carriers, and to the growth of malaria parasites therein.

Importance of the study of the life-history of mosquitoes.—A sound working knowledge of the classification, structure, habits and life-history of mosquitoes is accordingly indispensable to all medical men and women practising in India, and especially to all sanitary and malaria officers. The latter two groups of officers must likewise be familiar with all measures employed in the reduction of mosquitoes on a large and small scale, for without this knowledge the direction and supervision of anti-mosquito work cannot be carried out efficiently. If opportunity for a systematic course of mosquito-entomology is not available, the beginner should endeavour to acquire a familiarity with the local species of Anopheles, getting an expert to help him. A knowledge of local adult and larval Anopheles and their habitats will enable a distinction to be made between locally breeding species and invaders.

In India mosquitoes transmit to man malaria parasites, *Filaria bancrofti*, the unknown germ of dengue, and possibly other diseases; and they everywhere give rise to loss of rest and comfort, and add to the wear and tear of life.

Anophelines the only known carriers of human malaria.—There is no evidence at present that mosquitoes other than anophelines can act as hosts of malaria parasites; though we cannot definitely assert that some species of Culex, and even some of the group Aedes, which are so universally represented in India, may not do so. We do know positively that certain species of Culex cannot carry human malaria, and that none have so far been shown to be malaria-carriers.

FACTORS REQUIRED TO PRODUCE MALARIA:—(1) *Anopheline mosquitoes.*—As far as we know, then, no other forms of mosquitoes, or other insect, can act as carriers.

(2) The *present or recent existence of cases of malarial fever*—including relapses and cases of malarial infection acquired in other regions who have come to the district.

(3) *External physical conditions*—climate, moisture, temperature and season favouring the attacks of the mosquito, suitable for its infection, and for further development of the sexual form of the malaria parasite.

[1] Excluding *A. subpictus* [Myz. rossii], which is not a natural carrier of malaria in India, although a vector in certain parts of Java.

at least some deficiency in the scaly investment of the abdomen, and from Megarhinini by the straight proboscis and altogether different scaling. The *eggs* are laid singly, are more or less boat-shaped, and float on the water owing to the presence of lateral air chambers. The *larvæ* have no respiratory siphon, and when at rest lie horizontally just below the surface film of the water. The *pupæ* have trumpet-shaped respiratory siphons.

The Anophelini were divided into twenty-one genera by THEOBALD. Many of the genera differed so little that most authorities considered this subdivision unjustifiable, and have proposed a much simpler classification. For example, ALCOCK includes all the Anophelini in one genus—Anopheles, and this change is adopted by the writer.

The Anophelini are of particular interest to us as the only known group of mosquitoes that act as hosts of the parasites of human malaria during sporogony. But all species of Anopheles are not vectors; those that are, probably do not act as such with equal facility at all seasons and in all conditions; possibly also some of the individuals of carrying species are not susceptible
sleeping sickness after the introduction of *G.* in identical conditions. There
palpalis. ieties of malaria parasite do not
(ii) CLASSIFICATION OF ch carry malaria. There is wide

Bases of classification of mosquitoes. l investigation on these points.[1]
suggested for classification in the past, but it downwards like a hook. Free
were of quite secondary importance; the res completely covered with scales.
minor groups acquired undue importance and s posteriorly, proboscis, scutellum

In the early days of mosquito investigation
genera, the classification was based on the charied with the last two groups, they
sequently found, when many fresh genera were
were insufficient for a general classification, a interest; this genus provides the
species. Later the nature and arrangement
were used as a foundation for classification xidæ should form a third group of
study of the male genitalia and of the larvæ of times like mosquitoes, with almost
with the classification of the true mosquitoes. ler and are fringeless; the venation
ished by the existence of ventral

Number of known species of mosquit by its lying with its body bent like
1,000 mosquitoes have been classified and de er.
of the world. Comparatively few are con
majority are wild or sylvan mosquitoes, ar ATION OF ADULT MOSQUITOES
habits are not so well known as those of the d **ories required.**—Entomologist's
[illegible]; a few spare net bags to replace those torn during work. A dozen test tubes and a dozen glass-bottomed pill boxes ($1\frac{1}{2}$ inches to 2 inches in diameter). Specimen tubes with corks. Entomological forceps with curved end for holding pins. Entomological pins, an ounce. Common or large entomological pins. Gun-wad punch, No. 20 bore. Very thick paper or cardboard (4-sheet Bristol board from which discs may be punched); a supply of discs should be ready at hand. Needles with cutting edge, mounted in handles,

[1] In his *Provisional List of the Anophelini* recently published (*Ind. Med. Res. Memoir*, No. 3, Dec. 1924), Lt.-Col. S. R. CHRISTOPHERS, C.I.E., O.B.E., has favoured the subdivision of the tribe Anophelini into one genus—*Anopheles*, with the following five sub-genera: *Anopheles*, *Bironella*, *Chagasia*, *Myzomyia* and *Nyssorhynchus*. He states: "Each of these is precisely determinable by the male genitalic characters, so much so that in no case yet recorded is there a single intermediate form known; nor is it easy to see how any of the known types could directly pass from one condition to another. These stems have a distinctive distribution, such as is seen, for example, in genera of mammals. The single species representing the peculiar form *Chagasia* is South American, that representing *Bironella* is from New Guinea. Of the remaining three sub-genera, each represented by numerous species, *Anopheles* is world-wide, *Nyssorhynchus* is purely Neotropical, and *Myzomyia* is unknown in the New World" (p. 4).

species live upon the blood of man, mammals or birds. They are divided into families. We are here only concerned with the family Culicidæ, which is characterised by having narrow wings with the posterior border fringed with scales, the veins bearing scales or hairs, and the costal vein encircling the wing.

ALCOCK[1] splits the CULICIDÆ into two sub-families—Corethrinæ and Culicinæ.

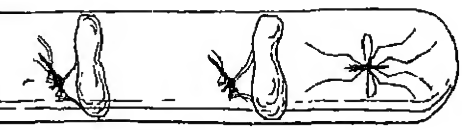
In the sub-family Corethrinæ the proboscis is short, bilobed and not adapted for piercing, and the palpi droop. They cannot bite man and animals, and do not transmit disease.

In the sub-family Culicinæ the veins on the wings are scaled, the proboscis is long and slender and, in the female, adapted in the vast majority for piercing.

The sub-family Culicinæ falls into four natural groups or tribes—Culicini, Anophelini, Megarhinini and Sabethini.

(iii) GENERAL CHARACTERS OF MOSQUITOES

General characters of Culicini.—Palps in the male as long as, or longer than, in the female, always mucler contains several insects (Fig. 5). Another shorter than the proboscis; metad or the finger under the test tube, rapidly notum nude, scutellum trilobec-wool. If a mosquito attempts to fly away When seen from above thesch it with the hand-net. Blank labels should mosquitoes appear much broadly; this is better than writing on the glass than Anophelini, and from a later aspect have a hunchbacked appearance. The *eggs* of *Aëdes*, thou laid singly, are never like those Anopheles; those of *Culex* a others are laid in rafts. T *larvæ* are provided with a r piratory siphon; when at r they lie obliquely in the wa with head downwards.



Collecting mosquitoes in a test tube.
JAMES's *Malaria at Home and Abroad.*

General characters ting is easily rubbed off. Mark on each tube **Anophelini.**—They range frose or hut in which the capture is made, and 3 to 7 mm. in length, excludii of course, be used for special notes.
the proboscis. Proboscis straighnear river-beds, pools and streams in the late well adapted for piercing. Palsons should work together. There will often be nearly as long as the proboscis ichwill alight on the clothes or exposed parts. the male and four in the female; the last two joints in the male are expanded. Antennæ plumose in the male, pilose in the female. Head clothed with upright forked scales, and a few narrow curved, and flat square-ended, scales at the sides in some species. Thorax and abdomen usually clothed with hairs which are never so plentiful as in Culicini. Scutellum simple. Wings in most species marked with black or brown patches; wing scales long and lanceolate or fusiform. The male mosquito looks very narrow when observed from above, and as seen in profile the long axes of the proboscis, thorax and abdomen form an almost straight line. When at rest on a flat surface the insect commonly presents the appearance of standing on its head with the body projecting away from the surface on which it rests. It should be remembered that *Anopheles* (Myzomyia) *culicifacies*, as its name implies, rests flat like a Culex. The female has only one spermatheca. The most favourable age for identification is one or two days. Anophelini are distinguished from Culicini and Sabethini by the simple curve of the posterior edge of the scutellum, and by

[1] *Entomology for Medical Officers*, by Lt.-Col. A. ALCOCK, C.I.E., F.R.S., I.M.S.

lid is rapidly closed; the cork is then removed, a little chloroform or benzene on cotton-wool or blotting-paper is inserted, the cork replaced. In a few minutes the night's capture will be found dead and may be removed and collected by overturning the box upon a paper placed on the ground. A lining of some black cotton stuff is preferable to simple blackening of the inside of the boxes. The captured anophelines may be put into an ordinary entomological bottle. Adult anophelines may also be bred out from ova and larvæ.

Adult mosquitoes may be rapidly stifled by tobacco smoke, or formaldehyde vapour, or by a few drops of chloroform on cotton-wool placed in the test tube or bottle. If it is required to use these bottles and test tubes subsequently for living mosquitoes, they should be thoroughly washed.

Out-houses, bath-rooms, damp go-downs, shaded verandahs, cow-sheds, coach houses, garages, stables, unoccupied thatched houses with dirty soot-covered walls, are special day resorts for anophelines. In a native village or bazaar select huts that are near a pond, water channel or other breeding place of mosquitoes. The searcher should cover his head and neck with a "Mosquinette" (Figs. 107, p. 396, and 108, p. 397), "Simpsonette" or other protection before going inside native huts, as some of the Anopheles will probably be infected with malaria. Some favour the thatch beneath the eaves of huts and houses and require a ladder to reach them. Anophelines are rarely seen on whitewashed walls in the day-time and seldom at night. They may often be found in holes in walls, or in the corners of rooms, under beds and tables, in cupboards, on dark clothes in rooms; behind pictures, doors, furniture, in open fire-places and chimneys, in lavatories; under porches and in sheds, under bridges and culverts, in wells and unscreened cisterns; they are fond of hiding in old boots (Wellingtons and polo boots *especially*), on saddles—leather seems to attract them. We may see them at night wandering about the shady side of the mosquito net. The wooden rafters of thatched houses are a favourite retreat. In such shady places they are readily captured as they are probably asleep, and it is usually easy to place the butterfly net or mouth of the test tube quickly and quietly over them. *The distribution* of some species of Anopheles is very local, hence it is necessary to examine as many likely places as possible.

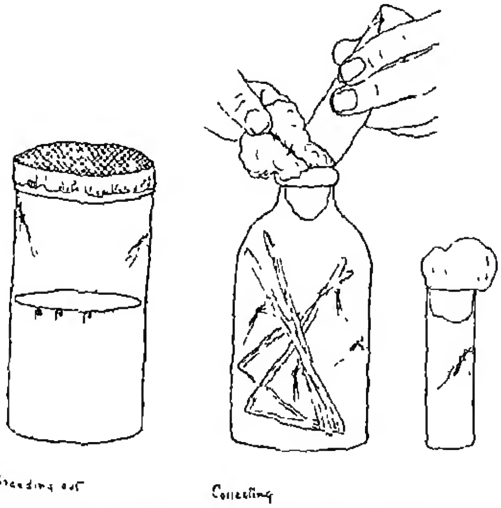


Fig. 6.—Method of collecting and breeding-out mosquitoes.

From STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed.

The mosquitoes when captured *in one of the* above ways are transferred to the large bottle by placing the open mouth of the test tube into it; the mosquito flies into the bottle, which is plugged again. In this way, when anophelines are abundant, about 30 *can* be caught in an hour. The writer has known as many as 65 caught in an hour with test tubes, with assistants to

three or four, for various purposes—dissecting, arranging legs and wings, etc. Cork carpet, a few sheets, about 6 inches square, on which to pin insects. Cotton-wool for separating insects in test tubes, packing mosquitoes when time does not allow of pinning, despatching insects by post. Cigar box, at bottom of which a cork carpet is fixed. Wide-mouthed, clear glass bottle, perfectly dry, for collecting mosquitoes. Long pencil and coloured grease pencil. An entomological box is useful, but not essential.

Mosquitoes may be collected in two ways—by capturing the adult insects and by breeding out from larvæ and nymphæ.

Capture of adult mosquitoes.—Test tubes and glass-bottomed pill boxes are useful for taking mosquitoes on exposed accessible places. When identification, breeding out and dissection are to be carried through, this is the best way to secure the adult insect. Place the test tube gently over the mosquito. Move the tube sideways; this disturbs the insect and it flies up the tube; then plug the open mouth of the tube with wool. With the long pencil push the plug down to within an inch or so of the bottom. Continue with other mosquitoes and plugs in the tube until the latter contains several insects (Fig. 5). Another way is to slip a piece of cardboard or the finger under the test tube, rapidly plugging the opening with cotton-wool. If a mosquito attempts to fly away when taking it in the test tube, catch it with the hand-net. Blank labels should be pasted on the tubes previously; this is better than writing on the glass

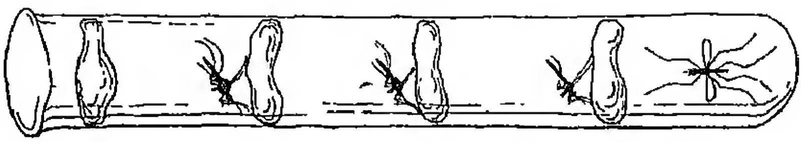


Fig. 5.—Method of collecting mosquitoes in a test tube.
From Lt.-Col. S. P. James's *Malaria at Home and Abroad.*

with the grease pencil, as the writing is easily rubbed off. Mark on each tube containing insects the station, house or hut in which the capture is made, and the date. The pocket book will, of course, be used for special notes.

Many captures may be made near river-beds, pools and streams in the late afternoon. In effecting this two persons should work together. There will often be swarms of mosquitoes, some of which will alight on the clothes or exposed parts of the body. The companion catches them in the tube; the hand-net will increase the "bag." Do not attempt to differentiate at once; this may be done later.

The writer has made more rapid captures by using small muslin butterfly-catching nets about 8 to 12 inches diameter, with a bamboo or cane circular rim at the top, and a short, 8 to 12-inch, handle. When required simply for counting relative numbers of different species of anophelines, or for dissection for sporozoite rate, this is a fairly rapid method of collecting anophelines. It is not to be employed when dealing with unknown species, as it leads to much rubbing off of scales and markings on wings, and may even lead to difficulty in identification of known species.

A simple and convenient method of catching anophelines, especially where they are few in number, is that of blackening the interior of packing cases provided with lids, each lid having a central hole for a cork. The cases are placed under beds and in dark corners of occupied rooms of huts and houses, in the evening, with the lid resting on the ground. In the early morning the

If for any reason the mosquitoes cannot be mounted, they may be preserved as follows: "Without pinning, place in a tube, separating one from the other by tightly fitting plugs of paper, so as to prevent any shaking. The mosquito can afterwards be relaxed with benzene."[1] Or, if in a hurry, they may be kept in match boxes or pill boxes if encased in cotton-wool.

Another method of mounting mosquitoes, especially in groups, is shown in Fig. 8.

A represents the mosquito impaled on cardboard. B. The mosquito impaled on a headless pin. C. One of the most convenient methods of examination of the mosquito is to use a stout cork (say that of a 3 in. × 1 in. specimen

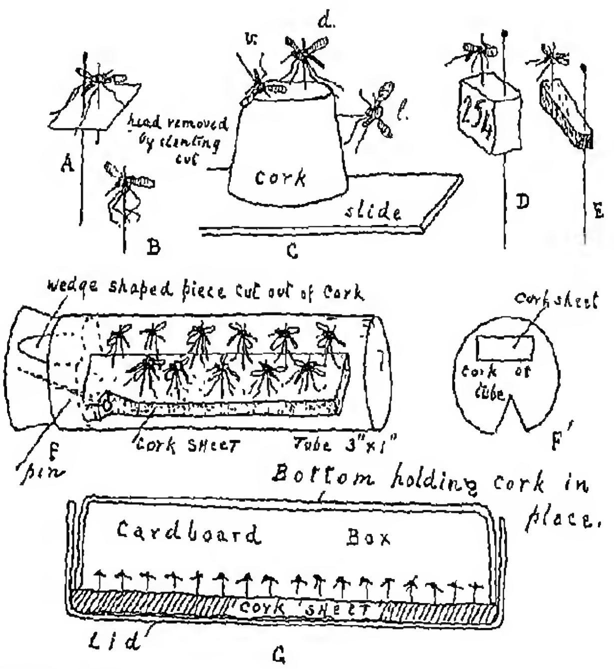


FIG. 8.—Shows a handy method of collecting adult mosquitoes devised by the late Lt.-Col. J. R. ADIE, I.M.S. Also illustrating the system of mounting, examining and preserving mosquitoes in use at the Central Malaria Bureau, Kasauli.

tube), which is placed upon a slide and manipulated with the mechanical stage. For examination of the dorsal (*d*) or ventral (*v*) surface the upper end of the cork is used; for lateral (*l*) and certain other views the pin of the mosquito is stuck at various angles into the side of the cork. D, E, G. The impaled mosquito with the thicker end of the pin driven into a block of pith, or a piece of cork, or stuck with similarly mounted mosquitoes on a piece of cork sheet, respectively. D also shows the remounted mosquito on a pith block after examination. F represents mosquitoes mounted on cork sheet in a specimen tube. F'. Before mounting the cork sheet, a wedge-shaped piece is cut out of the cork as shown

[1] Prof. R. NEWSTEAD, F.R.S., quoted in STEPHENS and CHRISTOPHERS's *Practical Study of Malaria*, 3rd Ed., p. 135.

transfer the mosquitoes to the large bottle, and as many as 110 with a butterfly net. Examine captures in the test tubes. Look for females with swollen abdomens laden with eggs. The captured mosquitoes may be killed by pouring a few drops of chloroform on the muslin cap of the large bottle, then dislodged on to a sheet of white paper, and, when necessary, mounted.

Any captured Anopheles with fully matured ovaries should be placed alive in bottles (Fig. 6) and allowed to lay eggs. By placing one species only in each bottle the character of the ovum may be noted as well as of the adult. Some of the ova should be placed in fresh water for hatching, and the character of the larvæ and pupæ determined.

For the scientific identification of species the collection of mosquitoes requires the greatest care. They are easily damaged by any rough handling. Important specific characters are supplied by scales on the wings and legs; the scales should be protected from being rubbed and the wings and legs from injury. If this is not attended to the specimens may be worthless as regards description or identification. A needle should be used for moving them about and for arranging the wings and legs.

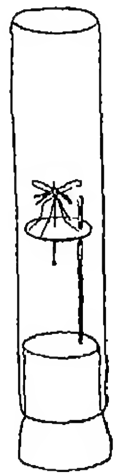


FIG. 7.
STEPHENS and CHRISTOPHERS'S method of preserving mosquitoes.

To mount adult mosquitoes.—Prepare a disc by cutting or punching out a circular piece of Bristol board or very thick paper with a scissors or gun-wad punch. Its diameter should be a little less than that of the specimen tube. On the under side of the disc write the data connected with the specimen to be pinned—locality (if necessary, altitude), date, collector's name, any special points of interest—although these are preferably written on an attached label, *e.g.* "the only local malaria-carrier," "the most prevalent anopheline." Push the fine silver pin two-thirds of its length through this disc. Place the mosquito on its back on a clean sheet of paper. For moving and steadying a mosquito always use a pin. Take the head of the fine pin between the finger and thumb, or hold it near the head with an entomological forceps. Place the point of the pin in the centre of the origin of the legs, which all arise very close together from the under surface of the thorax. Push the pin through the insect until it comes out near the centre of the back of the thorax and 1 mm. beyond by pressing it against the smooth surface of a cork or cardboard. The pin should not be pressed through too far, as it prevents the microscope lens being brought near enough for the examination. "Placing the disc against a cork, press carefully through the edge a stout pin. This is passed in the reverse direction to the fine pin. Force three-quarters of the length of the large pin through the cardboard disc, and then firmly press the point into the cork of a specimen tube, so that when the tube is corked the mosquito is inside (Fig. 7). Fix within the tube a plug of cotton-wool or some blotting-paper, soaked in pure creosote to prevent mould. If a collecting box is used, it should be moistened to the extent of making the cork show through the paper." Effort should always be made to collect two of each sex, and to prepare a description of the ova and larvæ.

The above is one of several methods for mounting permanent specimens. In field work we may perforate each insect with a silver pin (first cutting off the head of the pin with a scissors) and arrange them on a long strip of cork or cardboard, which is then placed in a specimen tube or test tube and the mouth plugged with cotton-wool.

there is (except just after cleaning) enough dust and moisture to form a film on the glass, which gives mosquitoes a foothold.

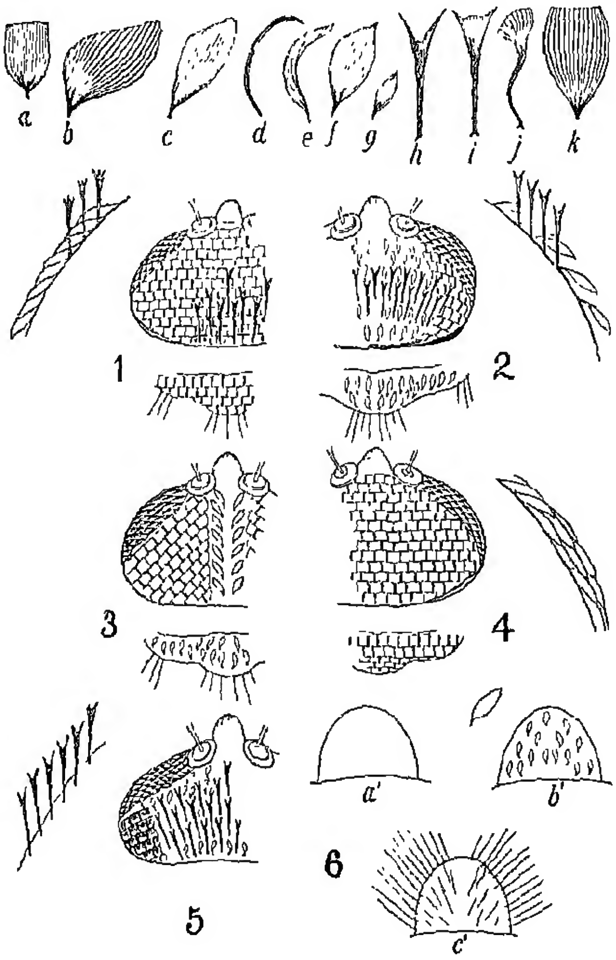


FIG. 14.—Types of scales, *a* to *k*; head and scutellar ornamentation, 1 to 4; forms of clypeus, 6; 1, head and scutellum of *Stegomyia*, etc.; 2, of *Culex*; 3, of *Aedes*, etc.; 4, of *Megarhinus*, etc.; 5, head ornamentation of *Cellia* and some other Anophelini; 6, clypeus: *a'*, of *Culex*; *b'*, of *Stegomyia*; *c'*, of *Joblotia*. (Theobald.)

From DANIELS and NEWHAM's *Laboratory Studies in Tropical Medicine*, 5th Ed.

Types of scales.—The following list includes the main types of scales of mosquitoes (Fig. 14, *a* to *k*).

(*a*) Broad, flat, spade-shaped, or tile-shaped scales.
(*b*) Broad, expanded, asymmetrical scales.
(*c*) Narrow, asymmetrical scales.
(*d*) Narrow, hair-like scales.
(*e*) Narrow, curved scales or crescents.
(*f*) and (*g*) Spindle-shaped scales.
(*h*) and (*i*) Upright, forked scales or darts.
(*j*) Long, twisted scales.
(*k*) Pyriform scales.[1]

[1] DANIELS and NEWHAM's *Laboratory Studies in Tropical Medicine*, 5th Ed., pp. 430, 437.

which ends near the tip of the wing. The *second longitudinal vein* arises from the first, and ends in two branches which form the so-called *first submarginal cell* (sometimes called the first *fork-cell*). The *third longitudinal vein* is simple and arises at or near the junction of *two transverse veins*, the *supernumerary* and the *mid*; this vein is of importance in identifying several species of Indian Anophelini. The *fourth* arises from the base of the wing and terminates in two branches which form the *second posterior cell* (or second fork-cell). The *fifth* also arises from the base of the wing and sends off a branch about half its length. The *sixth* is simple and arises from the base of the wing. Anophelines usually have spotted wings; *Culex* species mostly have unspotted wings.

Halteres or balancers.—These consist of basal swellings, a narrow stem and a swollen cup-shaped or funnel-shaped knot, which is usually scaly. They lie behind the wings and represent the hinder wings of four-winged insects.

Abdomen.—The abdomen consists of eight segments, in the *female* ending in *two lobes*, and in the *male* in *distinct genitalia*, consisting of *basal lobes*, *claspers* and various prominences. The male genitalia are useful for separating very closely allied species. Except in *Anopheles* the abdomen is more or less coated with scales, and may have lateral tufts of scales and bristles. Each segment has a row or rows of bristles along its posterior border and frequently many at the apex.

Legs.—The legs are long and slender, especially in *Anopheles*, and are attached to the pro-, meso- and meta-thoracic rings on the lower part of the pleura. Each

FIG. 13.—**Left**: Fore ungues of *A. funesta* (♂), the larger uniserrate. **Right**: Fore ungues of *A. subpictus* (♂), the larger biserrate. (After Theobald.)

From STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed.

leg consists of nine segments. The one at the base, by means of which it is attached to the body, is called the *coxa*, then comes a small segment called the *trochanter*, succeeded by the large *femur*, then the *tibia* and the *tarsus*; the last-named is made up of five segments, the basal one of which is much the longest. The femora and tibiæ are often bristly, and there may be spines on all the parts, which are always covered with closely appressed or outstanding scales. The fifth segment of the foot ends in two claws or ungues. It should be noted whether the banding in each tarsus, if any exists, is apical, basal or both, and whether well marked or slight, etc.; *e.g.* *A. jamesii* has the last *three hind* tarsi entirely white, *A. theobaldi* the last *two hind* tarsi white.

In consequence of their comparatively short legs the body of *Culex* species approaches the resting surface more closely than that of *Anopheles*.

Ungues.—(Fig. 13.) The ungues or claws are two in number to each foot; they are always *equal* in the *female*; in the *male* the fore and the mid pair are always unequal in size, whilst the posterior ones are the same in size. The ungues in the female may be simple or uniserrate; in the male the fore and mid ungues may be uni-, bi- or even tri-serrate. The ungues are in many species characteristic. Mosquitoes adhere to a wall just as a cat clings to the bark of a tree, by its claws. They cannot adhere to an absolutely smooth perpendicular surface in the same way as can a fly, whose foot acts as a sucker. We sometimes see mosquitoes on panes of glass; this is because on the pane

Indian Anopheles have they long hairs. The adult female may also have the abdominal cavity distended with eggs or blood.

Thorax.—The dorsum is covered with scales or hairs or with both; the character of these scales is to be noted.

Scutellum.—The *scutellum* is always simple in anophelines and *never trilobed* as is the case in other Culicidæ. It is provided with hairs or scales.

The **Post-scutellum** or *metanotum* is bare.

Halteres.—The knobs of the *halteres* are covered with many small scales.

Abdomen.—This important region has in some species very long hairs, but no scales. In other species, in addition to hairs a few scales are seen on the ventral surface of the last one or two segments only. In others, again, the dorsum of each segment is thickly set with white or golden brown scales, in some species very broad, in others more or less spindle-shaped.

Wings.—In Anopheles the wings are commonly dappled or profusely speckled, but are in some species spotless. Note the relation and position of the different dark- and light-scaled areas on each vein. The chief spots consist of groups of scales on the costal, sub-costal and first longitudinal veins. These spots are sometimes arranged in a characteristic manner as seen in the "T spot" of *A. subpictus* [M. rossii]. In all species variations are met with in these spots, and minor differences are insufficient to form a new variety, much less justify the creation of a new species. Variation is constantly seen in the imagines of anophelines bred out of the same batch of ova. Nevertheless the number and grouping of the spots are of some importance in diagnosing species. The small areas of scales found on the third to the sixth longitudinal vein are of use, and in describing an anopheline wing the arrangement of these areas should be given. The degree to which the third long vein is scaled is also of special significance. A complete description of a wing should include all the minute spots on it. The wing fringe possesses, at the points where the long veins intersect the margins, a variable number of pale areas. The shape of the wing scales is to be noted by examination of a wing under a cover-glass.

The legs.—The legs of anophelines are longer and thinner than those of other mosquitoes; in Anopheles they are about double the length of the body, whereas in Culex they are both about equally long. Like those of other mosquitoes, the legs consist of (1) *Coxa* and *trochanter*, which are small structures at the beginning of the legs; (2) *femur*; (3) *tibia*; (4) *tarsus*, which consists of five segments, the fifth carrying the *claws* or *ungues*. "It is necessary to make a careful examination of the markings on each leg, beginning with those on the femur and ending with those on the fifth tarsal segment." The various tarsal segments may be banded or speckled and the banding may be apical or basal. In some species complete bands of white scales encircle the legs near the joints, and the position of these bands should be noted. In addition small patches of white scales will be found in some species on certain segments of the legs (*speckling*), and in others one or more of the terminal tarsal segments of the legs will be found to be white-scaled in their whole length. The femora and tibiæ may be speckled or unspeckled. Several species can readily be diagnosed by the number of white tarsal bands, which may vary from one to three and a fraction of the next segment. The species of the now obsolete genus *Cellia* met with in India may be recognised by examining the tarsi of the hind legs apart from the four white bands on the palpi.

The male genitalia.—The characters of the *genitalia in the male* are important in scientific classification of the different species. The parts of the genitalia are best differentiated by staining and mounting. Boil in 10 per cent. potash solution until sufficiently transparent. Wash thoroughly, stain, if

On the wings other types of scales, either lanceolate, long, narrow scales, pointed at the free end, or long and narrow with square free ends, are met.

Distribution of the different types of scales.—The *scales* of *the head* are usually in three forms—*narrow-curved*, *upright-forked* and *flat*. The *scales of the thorax* are *narrow-curved*, *hair-like-curved*, *spindle-shaped*, *flat* and *twisted*. No upright-forked scales occur on the thorax or abdomen. On the *abdomen* the scales are usually *flat*, but may be spindle-shaped, narrow-curved or twisted upright scales. The *scales of the wings* are very varied—narrow, straight, linear scales (*Culex*), short, broad, flat scales (*Melacoconion*), broad, straight scales (*Tæniorhynchus*), very broad, flat, asymmetrical scales (*Mansonia*), and long and short lanceolate scales (many *Anopheles*, etc.).

The scales of the *wing fringe* are of three series—long and short fringe scales which are pointed, and small border scales which vary in form, some spatulate, others of the Mansonia type. Each vein has median scales, which usually differ in form.

A knowledge of scale structure helps in separating species, and in distinguishing species which to the naked eye seem the same, *e.g.* *A. maculatus* (p. 110) and *A. willmori* (p. 113), and also in the use of the synoptic table (p. 96 *et seq.*).

To study the scales.—(Fig. 14.) (*a*) Detach the part of the mosquito the scales on which it is desired to examine. Lay upon it a cover-glass. Tap and press the cover-glass lightly, then remove it and sweep away the fragment of mosquito. Replace the cover-glass and fix in position with strips of gummed paper. (*b*) Smear a slide thinly with glycerine jelly. Press the part with scales on the glycerine jelly. Add more jelly and cover.

Examination of Anatomical Structures of Anophelines

The first step is to be quite sure that we recognise anophelines when we see them. As noted, the body in repose is inclined at an angle with the resting surface; but *A. culicifacies* rests like a Culex.

Examination of proboscis, palpi and antennæ determines whether the insect is an anopheline or not, and its sex. In the anopheline the proboscis is straight and the palpi are as long, or nearly as long, as the proboscis.

Head.—Note the character of the scales, especially the upright forked scales. In most anophelines a prominent tuft of white hair will be seen projecting forward from the anterior part of the head.

The palpi.—The palpi are long and spatulate in the male, as long as or not much shorter than the proboscis in the female; they are composed of four segments. The banding of the palpi by white scales is most useful in recognising species. The apices of the palpi are generally white, but they are dark in *A. turkhudi* and *A. theobaldi*, var. *nagpurensis*. The number of bands on the palpi, their width and distance apart, whether the two apical ones are of equal width to the other palpal bands, etc., are of some significance. In this connexion we should not forget the differences that occur in the same species, even from the same batch of eggs, nor that seasonal variations likewise occur. We look also for white-scaled patches on the segments of the palpi—these are important.

Antennæ.—Note whether these are densely covered with scales or not, whether all of one colour or adorned with white bands, and if banded the number, position and relative size of the bands. In the *male* the *antennæ* are covered with long hairs having a plumose appearance, seen with the naked eye in front of the head. In the female the antennæ are almost bare ; in no

into a jar, be supported by the shoulder of the jar. Fill the stopper nearly to the brim with water. Cut a thin slice of cork and place it on the surface of the water. Place a piece of white paper on the cork. The paper should not occupy all the space in the mouth of the stopper. Now invert the chutney jar over the top of another jar, with a cardboard cover, in which some mosquitoes have hatched. Remove the cardboard lid and gently tap the glass; the mosquitoes will fly upwards into the jar. Place it upon its stopper (Fig. 16). After labelling, put the jar in a dark cupboard or other convenient place (incubator). At the end of the first day or so the males will be found dead upon the paper and can be removed. On the second night after hatching, most of the insects will feed and the jar is ready for use.

Place the inverted jar over a bottle containing Anopheles caught in a village or bazaar. Remove the cotton plug and shake the bottle gently to drive the insects out. Place in a dark spot. Next morning remove the stopper and any dead mosquitoes and ova by taking out the piece of paper.

Mosquitoes caught in a village or bazaar can sometimes be transferred to these stoppered jars. On the second night after their collection the bottle is ready for feeding experiments. On the third day, generally, the insects have no longer any blood remaining in the mid-gut, and are ready for dissection. The salivary glands of any that die before this may, if necessary, be dissected to see if sporozoites are present. Anopheles caught in native huts may, of course, give rise to a fresh infection in those on whom they are fed.

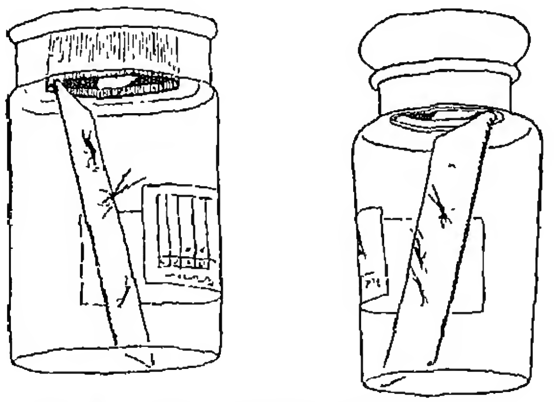


FIG. 16.—Method of keeping mosquitoes alive. From STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed.

Regarding this method STEPHENS and CHRISTOPHERS[1] state: "The advantages of the above way of keeping mosquitoes are that they keep alive longer than any other way known to us; the immense convenience in feeding; any mosquitoes that may have died in the night can be recovered, and are not dried up; it is an extremely convenient way of obtaining and examining the ova; mosquitoes which have become feeble are given the best possible chance of living and will be found resting all day on the piece of paper." When net-covered cages and boxes are used the death-rate is very high; the dead bodies dry up and are lost or damaged in the folds of the netting. The method described may be variously modified, and when a hollow glass stopper is not available any wide-mouthed jar will answer, using the strip of cardboard inside the bottle and inverting the bottle over a saucer containing a few teaspoonfuls of water.

To breed out mosquitoes.—Collect a considerable number of full-grown larvæ and nymphæ from all possible sources, including those of anophelines and culicines; the latter will greatly predominate. Separate the nymphæ from the larvæ and place them in a jar or wide-mouthed bottle half full of water. Cover the jar with thick cardboard or a lid the central part of which is replaced by

[1] *Practical Study of Malaria*, 3rd Ed, pp. 92, 93.

required, with a saturated solution of (basic) fuchsin. Wash. Dehydrate, clear and mount in balsam as for sections.[1] Liquor potassæ with a little peroxide of hydrogen also clears. Other chitinous parts, such as the proboscis, may be similarly stained and mounted.

The general type consists of two large fleshy basal lobes each with a terminal chitinous clasp segment, always curved and often ornamented with spines. Between the claspers, arising internally and ventrally to the claspers, are other chitinous processes, the *harpes*, which may be well developed, formed of two segments, or rudimentary. Between the harpes and the claspers are a pair of clasping organs, the *harpagones*. The chitinous lobes above the cloaca, the setaceous lobes, are parts of the rudimentary eighth segment. Each of these parts presents great variations in different species. It is necessary to examine them in the dried specimen, to see the relative positions of the parts, as well as in the cleared specimen (Fig. 15).

Other points of some significance are the position of the cross veins in the wings and the characters of the ungues.

The most satisfactory way of acquiring familiarity with the different species of anophelines in a locality is that of breeding them from ova and larvæ. Some of the known species of Indian anophelines can at once be recognised by examining the wing, the bandings on the legs, and the bands on the palpi, but a hurried examination of the wings and legs may not only lead to error, but to the non-recognition of new species. In describing an anopheline the position, number and dimensions of the pale bands (if any) on the palpi and on all the last tarsal joints, any adornments in the shape of white lines or groups of white or coloured scales on the body, and the markings on the costal borders of the wings in the shape of groups of white scales, should be given. Anophelines are often called the dappled or spotted winged mosquito, and "marsh or swamp mosquito," which are not altogether correct descriptions, as there are anophelines without spots on the wings, and anophelines breed in other places besides swamps; nevertheless these appellations show two of their commonest peculiarities. All anophelines that carry malaria in India have spotted wings, and most anophelines prefer breeding in swamps.

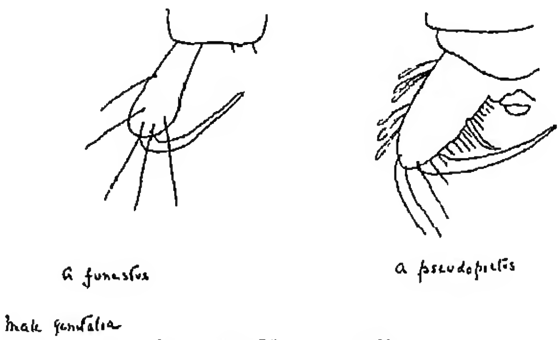


FIG. 15.—Male genitalia

From STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed.

The number of species of anophelines in any particular place under investigation is fortunately small, and the difficulties of identification therefore easily overcome. The maximum number of anopheline species found by the writer in any one station was eight; six of these eight were bred out from the Tons and Nun Rivers in Dehra Dun between October 11 and 16, 1909.

To keep mosquitoes alive.—The length of time mosquitoes live in captivity depends largely upon the suitability of the conditions in which they are kept. Get some glass chutney jars with hollow glass stoppers or other glass jars of the kind. Cut a piece of thick cardboard of a size that will, when put

[1] STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed., p. 144.

themselves to the position of the very powerful thoracic muscles which propel the wings (Fig. 18). The glands are surrounded by *fat-bodies*, and are very large in proportion to the size of the mosquito. The three lobes of each gland are composed of acini of the same structure.

In Anopheles the ends of the ducts in the lobules are dilated, while in most other groups the ducts are of the same calibre throughout. The lobules may bifurcate.

To dissect out the salivary glands.—For the dissection the *accessories required* are: two cutting needles mounted on light wooden handles, slides, cover-slips, normal saline solution, dissecting lens, microscope with a ½- and a $\frac{1}{6}$-inch lens.[1] Chloroform some mosquitoes in a test tube. Select a female. Take off the wings and legs. Place the insect on a slide in a drop of normal saline solution on its left side, head towards you, on a black background. Place the left-hand needle on the thorax to steady it, and make the soft parts about the neck bulge, and the right-hand needle on the back of the head, and make gentle traction with the right hand towards you. The salivary glands are intrathoracic; begin at the hinder part of the neck and end opposite the first pair of legs; and lie ventrally. Under a ½-inch lens with the diaphragm almost closed, or under a dissecting lens, it will be seen that the glands are by this method dragged out attached to the head—the head pulls out a little mass of white tissue from the thorax; the glands are seen attached to the neck as a finger-like, glistening white semi-transparent mass, and appear as two little bodies with three lobes in each (Fig. 18). Next place one needle on the head and with the other cut across between the head and the attached portion of the glands. By this method all six glands are obtained free from neighbouring structures, but if necessary they may be teased out further and placed in a fresh drop of solution. If the glands are not seen as refractile bodies in the mass, press again with the needle lying on the thorax and with the other needle scoop out such tissues as present themselves easily at the opening from which the head has been torn. If not actually included in the portion secured from the neck, the glands will be found in the piece of tissue last extracted. Remove the head to another slide and the thorax to a third; the salivary glands are on the first slide alone. Put on a cover-glass and examine with a $\frac{1}{6}$-inch lens. Press the cover-glass with the point of a needle and express secretion. Sporozoites, if present, will be seen in large numbers as fine, distinct curved rods. The course of sporozoites in mosquitoes from the stomach to the salivary glands is no instinctive directional migration. Sporozoites are dispersed throughout the body. There is a veritable septicæmia of them in, at all events, benign tertian and malignant tertian parasites. There are other ways of dissecting out the salivary glands, but the writer has found this one simple, rapid

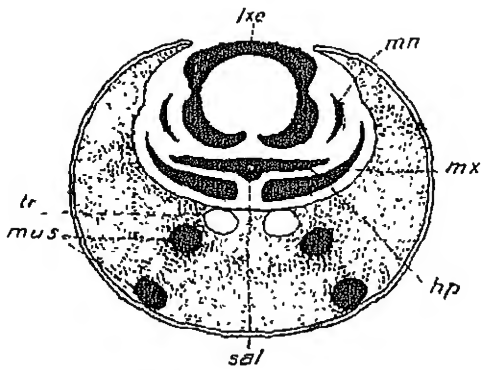


FIG. 17.—*lxe*, Labrum-epipharynx; *mn*, mandibles; *hp*, hypopharynx; *sal*, salivary duct; *tr*, trachea of labium; *mus*, muscle of labium; *mx*, maxilla.

From DANIELS and NEWHAM'S *Laboratory Studies in Tropical Medicine*, 5th Ed.

[1] A *dissecting microscope* is useful, although not indispensable.

mosquito netting. Put the larvæ in a well-lighted but not a hot place. The length of larval life varies, even in the issue of eggs laid on the same day and of larvæ of the same species reared under identical conditions. Remove the nymphæ as they are seen at the end of each day. Or place twenty or thirty full-grown larvæ or pupæ in the water in which they were found in a finger bowl, and cover it with a piece of gauze supported on a framework of wire. In a few days the adults will be found on the gauze. They may be fed on glucose solution on cotton-wool, or a thin slice of banana may be put on the gauze to feed them. The winged insects should not be killed for a day to allow them to develop. Let the insects escape into a clean, dry glass vessel or jar. Pour some chloroform on a wad of cotton-wool and place it under the jar. The chloroform itself should not touch the mosquitoes. They may also be killed by tobacco smoke or concussion. Some workers prefer using a cyanide jar for killing mosquitoes. Do not remove the insects for a few minutes after they fall. Turn them out upon a sheet of clean white paper. There are usually more males than females in the bred-out mosquitoes. It is said that if larvæ are supplied with abundance of food the proportion of males is much reduced.

(vi) Internal Anatomy of Mosquitoes

Dissection of mosquitoes being imperative in the practical investigation of malaria, we must know the normal anatomy of their internal organs and how to find malaria parasites in them.

Dissection of mosquitoes.—We require slides and cover-glasses, two needles with cutting edges and some salt solution (0·5 per cent.). It facilitates dissections considerably to have a white and black background to work on. Pieces of black and white marble or glass (6 inches square) let into and fixed in the working table are easily improvised (vide infra, *To dissect out the salivary glands*).

Some mosquitoes are caught—by placing over the top of the jar for feeding (pp. 73, 74) another empty jar of the same size—and kept alive in a dark cupboard for two or three days, until their stomachs are quite free from blood. Kill a few specimens. The simplest way of doing this is to "knock it on the head" by rapping the test tube containing it smartly over the knee; incidentally, this procedure shingles the scales of the insect. Observe, if a gravid female, two whitish areas on either side of the hinder portion of the abdomen (ripening ovaries). If the blood in the stomach be not digested, a dark mass will be seen in front of these, and possibly the extreme anterior portion of the abdomen will appear transparent. The *internal anatomy* of all mosquitoes is much the same; the following is a brief description of that of a female Anopheles. The main features are shown in Figs. 18 and 19.

Salivary ducts and glands.—The salivary duct is not connected with the alimentary canal. The saliva is ejected through the hypopharyngeal canal. At the base of the hypopharynx is a structure connecting the common salivary duct and the groove. This is a pump depending for its function on the powerful voluntary muscles around it. The common salivary duct ends in the centre of a chitinous membrane which is continuous with a highly chitinous cup opening into the hypopharynx. The duct passes back beneath the valve of the buccal cavity, where it divides into two ducts of similar structure. The two salivary ducts run parallel along the ventral wall of the neck into the thoracic cavity; on reaching this region they diverge and branch into the salivary glands. Each salivary gland consists of three blind sacs or lobules, which vary in position as the glands have to accommodate

the extreme end and pull gently. After separating the segments a very short distance, remove the preparation to a dark background. Again draw apart and note the white viscera stretching between them. Make steady traction until a central, rather transparent body is alone left between the two portions of abdomen. Cut across the anterior attachment of the mid-gut. Draw the body of the mosquito away from the separated segments; the mid-gut and sundry other viscera will be left attached to the latter, floating in the salt solution. Observe that when the tension is relieved, the structure last to leave the abdomen of the mosquito assumes a saccular appearance. This is the mid-gut. It extends from the line of the first pair of legs to the posterior border of the sixth abdominal segment. It consists of an anterior narrow part and a posterior dilated part at the level of the fifth and sixth abdominal segments. If any blood remains in this part of the stomach, use another specimen, one kept longer without food, as with blood it is difficult to see zygotes.

At the commencement of the mid-gut is the *proventriculus*, a thickened ring-like structure acting as a valve between œsophagus and mid-gut (Fig. 19).

Malpighian or urinary tubules.—Passing between the mid-gut and the separated segments, note the five brilliantly white thread-like Malpighian tubes. They lie freely bathed in the fluids of the hæmocele. They are looped anteriorly above their origins and their ends are held in position near the rectum by tracheal branches. They are lined with secretory epithelium. Their function is chiefly excretory.

Hind-gut.—Between the Malpighian tubules the transparent intestine is seen; it may display peristaltic action (Fig. 19).

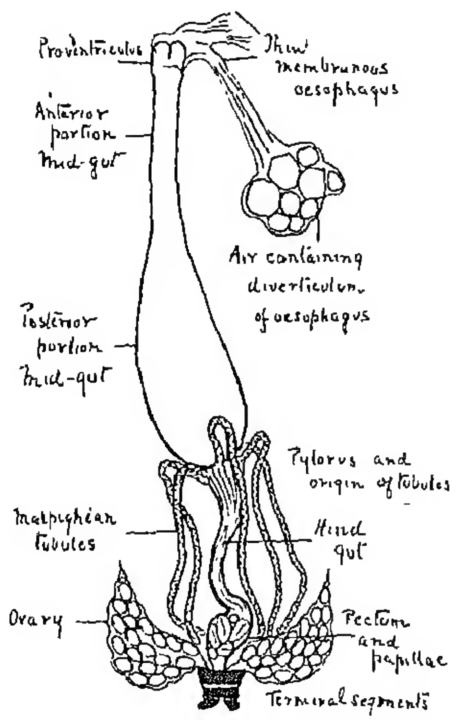


FIG. 19.—Dissection of the viscera of a female mosquito.

From STEPHENS and CHRISTOPHERS's *Practical Study of Malaria*, 3rd Ed.

To prepare the mid-gut for examination.—Cut across the intestine and Malpighian tubules just below the termination of the mid-gut. This separates the mid-gut from the other viscera. Remove everything from the slide except the mid-gut; no ova or extraneous matter should remain on the slide. Add a drop of salt solution and place a thin cover-glass upon the preparation. The mid-gut flattens out. Remove with filter paper applied to the edge of the cover-glass any excess of fluid. Examine under a $\frac{1}{6}$-inch objective and afterwards under a $\frac{1}{12}$. The following are now seen. The narrow anterior portion of mid-gut with the calyx-like proventriculus at its free end. The expanded posterior portion forms the main mass of the preparation; it is very important in relation to malaria parasites. A good preparation shows well-defined tubes with spiral lining (air tubules or tracheæ); note that these branch and ramify

and certain. Note that the glands of each side consist of three acini (Fig. 18), the ducts of which almost immediately join after leaving the glands to form a single long duct.

Alimentary canal.—The alimentary tract and its accessory organs, the stomach and salivary glands, are the most important parts for the present purpose, because in them, in anophelines, are developed the sexual forms of the malaria parasites of man.

The *alimentary canal* begins, it may be said, at the apex of the proboscis and ends at the terminal anus. A *pumping organ* sucks the blood up through the tube formed of the labrum and hypopharynx (Fig. 17). "Almost, if not quite, coincidently with the moment that the skin is pierced, a small amount of saliva is injected through the epipharyngeal groove into the wound, and suction begins very soon after that. The pumping portion, the fore-intestine, regularly contracts and expands, drawing the blood from the victim into the mosquito's body. Unless disturbed, the creature will continue to feed until its abdomen is distended almost to bursting."[1] Behind the clypeus the different mouth parts unite to form what may be considered the *mouth*. Following the mouth is the *buccal cavity*, which opens into the pharynx by a valvular arrangement. The *pharynx* or pumping organ extends from the buccal cavity through the head or near the back of the head, where it joins the œsophagus. At its commencement it is tubular, but lower down dilates; it is much larger in the female than the male; it is partly chitinous. The œsophagus extends from the pharynx to the so-called *œsophageal valve*. Running from the œsophagus are three large blind sacs—food reservoirs or *diverticula*, one ventral and two latero-dorsal. The walls are often wrinkled and the cavities may contain sporozoite-like crystals of unknown nature. The large ventral reservoir extends back to the seventh segment when filled with blood or vegetable fluids. The valve lies between the œsophagus and mid-gut.

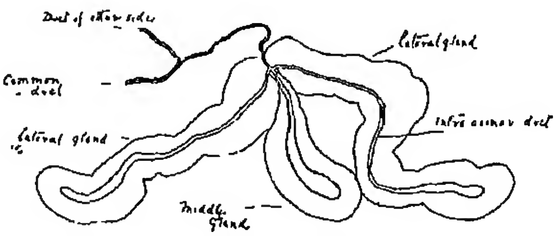


FIG. 18.—The salivary glands of one side.
From STEPHENS and CHRISTOPHERS's *Practical Study of Malaria*, 3rd Ed.

Mid-gut (stomach).—This is the largest part of the alimentary canal, and consists of a straight tube running from the œsophageal valve to near the end of the body (that is, about the level of the sixth abdominal segment). *The stomach itself is the posterior dilated part of the mid-gut*, and it is in it that malaria parasites develop (Fig. 19).

The *hind-gut* begins where the Malpighian tubes arise. It is short, slightly flexed, and ends in the anus.

To dissect out the mid-gut.—For the dissection the accessories required are, as before, two cutting needles on light wooden handles, a fine sable brush, chloroform, normal saline solution, some slides and cover-slips. Suppose we have a mosquito in a test tube. Kill it by a whiff of chloroform or concussion. Pull off with the forceps the legs and wings. Place the mosquito in a drop of salt solution on a slide and place the slide on a light background. Turn the insect on its back and with the needle make a nick in the chitin on both sides as near the "tail" end as possible. Now place one needle on the thorax and the other on

[1] HEADLEE, *The Mosquitoes of New Jersey and their Control.*

They float on the surface of the water. If submerged for any time they fail to hatch out. They are laid at the water's edge, on floating objects, or on the water itself, and are provided with a mechanism to enable them to flo[illegible]rtain [illegible]dapt themselves to extremes of[illegible]

lay their eggs in quite dry p[illegible]mersed. In *Anopheles* and some species of *Aedes* each ovum is separate in the water and is provided with air cells to keep it afloat. With *Culex* and *Tæniorhynchus* hundreds of ova are cemented together and form rafts, each egg resting perpendicularly, large end downwards; in the former the rafts are broad and oval, in the latter long and narrow.

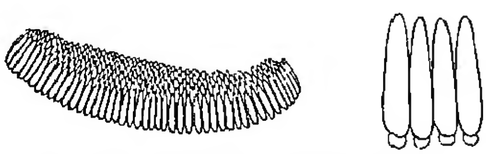


Fig. 22.—Egg raft and eggs of Culex.

In some species eggs remain dormant throughout the winter, in others they do so in the dry weather. Normally eggs hatch out in one or two days, sometimes within twenty-four hours, and the larvæ proceed to feed voraciously. The whole process from egg to imago in India during the breeding season is carried out in from seven to ten days.

Ova of Culex.—(Figs. 21 and 22.) Search at the edge of a dirty-looking pond

Fig. 23.—Eggs of Stegomyia.

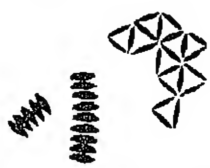


Fig. 24.—Patterns formed by eggs of anophelines

From Stephens and Christophers's *Practical Study of Malaria*, 3rd Ed.

or pool for egg rafts. They will be found mixed up with disintegrating vegetable débris, leaf-stalks, etc. They are readily seen, and are of blackish brown colour and easily blown about on the surface. The raft is boat-shaped, about $\frac{1}{8}$ to $\frac{1}{4}$ inch long, and contains from 200 to 400 eggs. The individual ovum is a smooth,

upon the surface of the mid-gut and Malpighian tubes; observe the large muscular fibres together with elastic fibres, forming a meshwork. Note that they [illegible] circular and longitudinal (external) and that at the edge of the viscus [illegible] Note also large cells with [illegible]

branch throughout the body. [illegible] other trunks running longitudinally, one on each side, sending branches (or other divisions) to various organs and to the *spiracles*; large branches go to the thoracic spiracles, short, stouter ones to the abdominal spiracles.

The vascular system.—Within the exoskeleton of the mosquito is its body-cavity or *hæmocele*, communicating with the *dorsal vessel* which represents the heart. The dorsal vessel is a delicate-walled tube composed of longitudinal and oblique fibres, with a nucleated inner layer. The fibres may be traced directly from the terminations of the branched alary muscle fibres. The alary fibres break up into fibres which are closely connected with the large pericardial cells, and eventually form (1) fibres passing into the dorsal vessel as longitudinal fibres, (2) fibres joining in an anastomosis in connection with the floor of the dorsal vessel. The pericardial cells are extremely large cells lying on either side of the dorsal vessel throughout its whole length. They vary from 80 to 50 μ in long diameter. They appear to be ganglion cells.

Genital organs—ovaries.—In the *female* the genital organs consist of the two *ovaries* opening into a common duct by the ovarian tubules (Fig. 19). Into the common tube opens a mucous gland, and also, by a long thin duct, the *spermatheca*, a chitinous sac, acting as reservoir for the spermatozoa. If the mosquito is not newly hatched out, the ovaries are seen as two opaque white bodies connected with separated segments; if near maturity they show masses of white eggs.

The male genitals consist of two testes united by *vasa deferentia* to the ejaculatory duct, to each vas deferens is attached a short sac, the *receptaculum seminis*. The penis is soft and muscular and is placed between two internal claspers, etc., and on each side of these are large *external claspers*, which are of diagnostic value (Fig. 15).

(vii) Ova of Mosquitoes

The ova of mosquitoes are small bodies 1 mm. or less in length. At first white, they soon become brown or black. The form and structure, number deposited and the way in which they are laid vary with the species or genus.

surface very narrow, the frill being continued uninterruptedly round this surface, and the lateral floats not touching its margins. *Anopheles culicifacies* and *A. listonii* eggs are of this type, which have in most cases been found in open natural waters or running streams. *Type II:* Ova having

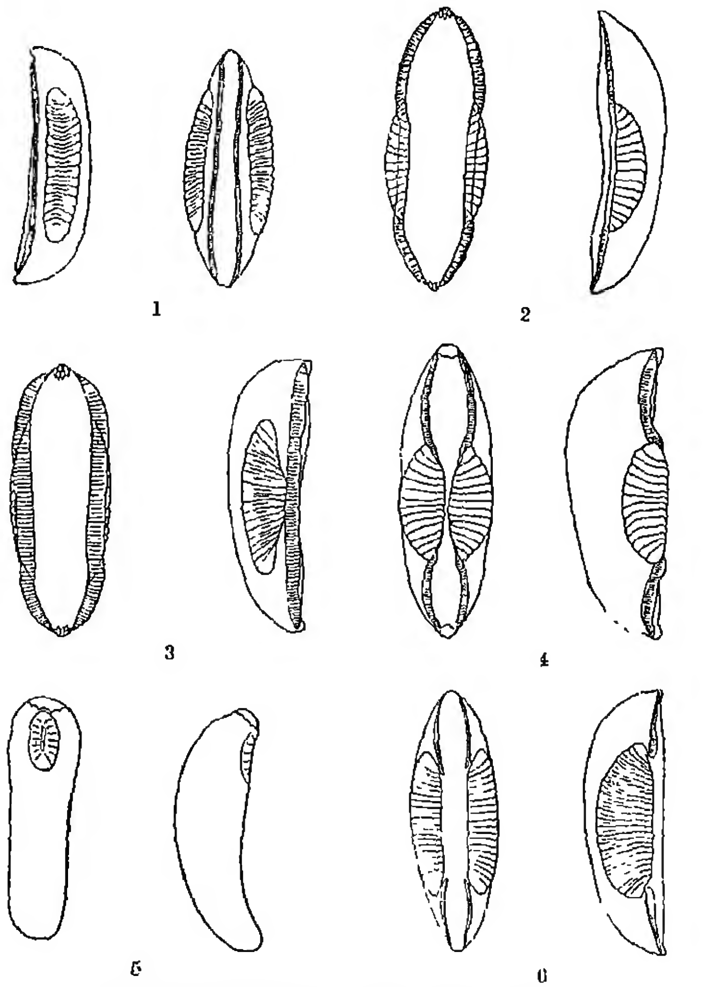


FIG. 25.—Ova of various species of Anophelini.
1. *A. culicifacies* 2. *A. pulcherrimus* 3. *A. subpictus*
4. *A. stephensi* 5. *A. turkhudi* 6. *A. maculipalpis*
From STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed.

a more or less broad upper surface with the lateral floats touching its margins and apparently arising from the frill. *A. subpictus* [M. rossii], *A. fuliginosus* and *A. stephensi* eggs are of this type. These are mostly found in pools. *Type III:* Ova with no lateral floats. Only one species of this type so far discovered in India—*A. turkhudi.*

elongated body of from 0·7 to 0·8 mm. in length. There are no floats. Observe that one end is thicker and more obtuse than the other, and that at the thicker end is seen a clear, transparent structure—the *micropylar apparatus*. Collect different kinds of rafts and note, by the hatching of larvæ, whether they can withstand desiccation.

Ova of Anopheles.—Anopheles eggs (Figs. 20 and 24) are difficult to see in water, but if present at the edge of a likely pool are discoverable by skimming the surface with a mug and then using the hand-lens; often many will be seen at once (Fig. 20). They vary from 0·7 to 1·0 mm. long. Place several female Anopheles with mature ovaries in a bottle (p. 74). Note that 50 to 150 ova are laid (the average in captivity is 120). Remove the piece of paper upon which the ova are deposited and place this upon a slide. Examine under the microscope with a low power in strong daylight without the mirror. The upper surface of the egg is flat, the lower convex, and one end (which contains the head of the embryo) is stouter than the other. Note the resemblance of the ova to little boats and the presence of two beautiful oval air cells placed upon either side acting as *floats*. The floats consist of a number of air chambers which vary in size and shape in different species and occasionally extend all round the egg, *e.g.* in *A. plumbeus*, or are reduced to very rudimentary structures, as in *A. turkhudi*. Note the white *frill* or a mere ribbed rim around what would be the gunwale of the boat. There is a micropylar process at the end of the egg encircled by a relatively large rosette formed by a material precisely similar to that which forms the lateral floats. At the opposite end of the egg there are also three or four plate-like extensions (NEWSTEAD). The eggs of Anopheles are laid singly, and float singly, or barely touching, in groups. Some species form starlike, triangle or parallel patterns,which patterns depend on physical conditions. Disturb a collection of eggs in water and watch the patterns re-form. Eggs are white when laid, soon becoming darker, and finally black. They are often laid in an irregular mass, which breaks up and forms patterns. Put some half-dried mud in a flat dish inside a piece of mosquito netting in which are some Anopheles with ripe ovaries. Note that the ova are laid upon the mud. Keep the mud for forty-eight hours, but do not allow it to get quite dry. At the end of that time remove a few ova on a dry slide and place under a low power. Let a drop of water flow over the ova. Note the escape in one or two minutes of young larvæ from the broad end of the ovum. Anopheles in a test tube will sometimes lay eggs on the side of the tube. Note the time the eggs are laid, and the time the larvæ escape; this depends largely on temperature. It may take two or three days. Place some ova on paper and let them dry; note that after two or three days (86° to 96° F.) at the most they will not hatch out when put in water. Great care should be taken that all the mosquitoes in the jar are of the same species; if more than one species are introduced, it will not be possible to tell to which species the eggs belong. We do not know what conditions of dryness the eggs of various species of Anopheles in India withstand, nor how long the eggs retain their vitality. Freshly laid eggs cannot withstand drying, but older eggs, in which embryonic development has made some progress, can retain their vitality in air for seventy-two hours. Sometimes Anopheles lay brick-dust-like masses of eggs; these do not develop to larvæ.[1]

The alleged transmission of malaria through the eggs of infected anopheline vectors is not credited, but observations on a scientific basis refuting the statement are very few.

Types of Anopheles eggs.—(Fig. 25.) *Type I:* Ova having the upper

[1] STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed., p. 186.

abdominal segment bears below a fan-shaped arrangement of long hairs. The neck of the anopheline larva is very slender and the head can be turned upon the body. The larva finds its food on the surface, and gathers it by the constant motion of little broom-like processes projecting from the sides of the mouth. To get its mouth to the surface, while maintaining its position for breathing, the head is turned half round on the body, which position is impossible to larvæ of other groups of mosquitoes. The larva becomes a pupa in about ten to twelve days. Pupation usually occurs at night. In from two to four days or more the pupa becomes an imago or full-grown anopheline. Anopheline larvæ differ from all others in that the stigmata or breathing tubes open directly on the surface of the eighth segment, and not at the end of a chitinous tube. The openings are in a depression surrounded by small chitinous plates, which almost close over them when the larva descends into the water. Anopheline larvæ change their position at the surface of the water by a series of very characteristic jerky, darting movements in a backward direction.

Larvæ removed from water but kept in moist air succumb. Pupæ removed on blotting-paper and kept in a moist-air chamber survive and fulfil their term.

Regarding specific identification, the head patterns (Fig. 29) vary very much and cannot be relied on. The frontal hairs (Figs. 36 B, 37 B, 38 B), and antennæ (Fig. 33) are the most dependable structures. The palmate hairs (Fig. 31) also vary a little; *e.g.* both *A. subpictus* and *A. stephensi* larvæ may have well-developed palmate hairs on the first abdominal segment, and very occasionally rudimentary ones in the thorax. The colour of larvæ is of no use for identification, it depends on the nature of the food consumed. The writer has seen *A. subpictus* larvæ of a vermilion red, dark green and light yellow—the head always being black.

Larvæ may be examined under a low power on a slide with or without a cover-glass; but this last keeps them from wriggling about. The chief structures to which attention should be directed are all of specific importance, and considered further below—the antennæ, clypeal or frontal hairs, leaflets of the palmate hairs, their terminal filaments, and the segments which carry them.

Freshly hatched anopheline larvæ are minute structures with tiny black heads and transparent bodies, rapidly wriggling on the surface, and easily distinguishable with a hand-lens from those of other mosquitoes.

In early life these larvæ normally remain just beneath the surface, and even when of moderate size seldom go to the bottom (anopheline larvæ do not like deep waters). The specific gravity is nearly equal to that of water—the tension of the surface film affords all the support they require to enable them to float. The body is held parallel with the surface, and just below the surface film so that a part of the head and the two breathing orifices on the eighth abdominal segment are out of the water. In *A. turkhudi* larvæ, when about to change into nymphæ, the head gradually sinks, and the tail only touches the surface. As has been noted, the head rotates on the neck so that the larva can turn it round with the greatest of ease, and it habitually feeds with the under surface of the head towards the surface of the water. The long fringes of the mouth, "the feeding brushes," are constantly vibrating and causing inward currents towards the mouth, so that all particles in the neighbourhood are drawn towards the mouth at a rapid rate—spores of algæ and tiny particles of all kinds are thus taken into the digestive tract, and under a low power lens may be seen in the living larvæ passing through the head into the thorax. In both the larval and pupal stages air is needed; to obtain it the breathing tubes must at frequent intervals protrude from the water surface into the air above. A film of oil placed on the surface of the water can prevent

hairs, especially at the sides. The *abdomen* is slender and is made up of nine segments. The first seven are very similar, with simple and compound hairs at the sides, and on both dorsal and ventral surfaces; also long lateral hairs, some of which are feathered. The eighth abdominal segment bears the *respiratory openings* or *stigmata* and the *lateral combs*. The stigmata are placed laterally and from them two chief air tubes run along the body, ending blindly about the middle of the thorax. All larvæ rest in such a position on the surface of the water that the respiratory opening located near the tail is in direct communication with the air. The lateral combs consist each of a group of separate, variously shaped chitinous scales; they are specialised in Anopheles. The ninth segment is small, directed downwards and ringed with chitin. At its extremity it bears four cylindrical processes, the tracheal gills surrounding the anus. These vary in shape and size in different species, larvæ which feed at the bottom are richly supplied with tracheæ. Along the middle line of the ventral surface are many compound hairs, which form a long steering arrangement—the ventral brush; dorsally at the apex a few long hairs project posteriorly." [1]

All mosquito larvæ go through four periods of development, casting their skin at the end of each period, and with the last moult becoming pupæ. The duration of the larval stage depends upon the species, food supply and temperature, and occupies in India a week in optimum conditions.

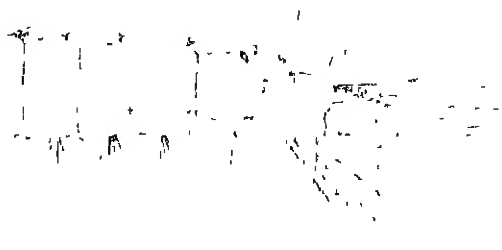


FIG 28.—Posterior extremity of Anopheles larva showing sessile stigmatic apparatus and palmate hairs.

From JAMES and LISTON'S *Anopheline Mosquitoes of India*, 2nd Ed.

Anopheles larvæ.—(Fig. 26, B.) The general structure of anopheline larvæ is peculiar and at once distinguishes them from the larvæ of other groups. The head is small; four bristles or feathered hairs project from the edge of the clypeus. It is provided with *frontal hairs*. These are of service in helping to diagnose the species but vary at different stages of the same species. There is no projecting respiratory tube or syphon, the body is provided with long lateral branching hairs, and upon the dorsal surface of a varying number of abdominal segments there is a pair of *palmate hairs*, each with a stalk and a conical expansion of fine hairs, the whole forming a very characteristic little fan-shaped structure. It is by means of these palmate hairs, which cling to the surface film, that the larva retains its horizontal position just under the surface. The number of pairs of palmate hairs and the segments on which they are placed are important in distinguishing the species to which they belong. The characters of the individual leaflets into which these hairs branch and their terminal filaments are also of specific importance. In the newly hatched larvæ the hairs are not branched or feathered and the cockades have the form of simple scales.[2] There are long lateral hairs on the thorax and abdomen, strongly feathered. The ninth

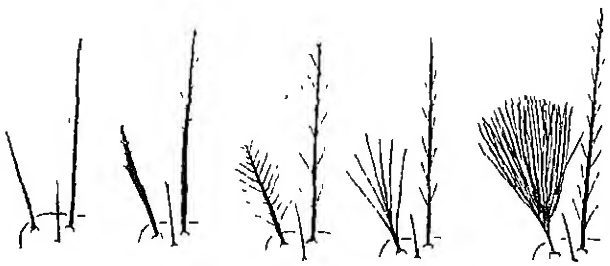
[1] H. F. CARTER, article, "The Blood-Sucking Nematocera," in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. I, p. 335.

[2] STANTON, quoted in ALCOCK'S *Entomology for Medical Officers*, 2nd Ed.

the back of the head. Grouped around this V mark are more or less continuous patches of pigment which show differences in their arrangement to some extent conspicuous.

The antennæ.—(Figs. 29 and 33.) At their terminations are two leaf-shaped bodies, and a branched hair arises between the leaflets. The antennæ are covered with small spines which are particularly developed in pairs along the inner border. In most anophelines a hair can be made out arising from a papilla situated at the junction of the proximal and middle third of the antenna; it is of specific importance. In the majority of anophelines it is simple and unbranched; in *A. barbirostris*, *A. nigerrimus* and *A. lindesaii* it is branched, especially in the former two (Fig 33).

The clypeal hairs.—These are four or six in number. Two spring from the extreme front of the clypeus near the middle line; two from the outer corner of the clypeus immediately over the feeding brushes, and two, usually very small and not always present, behind the origin of the others. These hairs are best seen when the feeding brushes are retracted. Do not confuse



1 2 3 4 5

Fig. 30.—Clypeal hairs of some Anopheles larvæ.

1. *A. subpictus*, *A stephensi*, *A. culicifacies*, *A. listonii*.
2 *A. maculipalpis*. 3. *A. jeyporiensis*. 4 *A. pulcherrimus*.
5. *A hyrcanus sinensis*, *A. barbirostris*.

From Stephens and Christophers's *Practical Study of Malaria*, 3rd Ed.

these hairs with certain other hairs on the head. These are: Six large branched hairs arising from the prominence lying between the bases of the antennæ and four similar branched hairs, but smaller, situated farther back (Nuttall and Shipley). These hairs exhibit great variation in different species, but are constant in the one species. The four anterior hairs may be quite simple and unbranched, *e.g.* *A. subpictus*, *A. stephensi*, *A. culicifacies*, *A. listonii*, *A. turkhudi* (Fig. 30). All four anterior hairs may show small lateral branches, *e.g.* *A. jeyporiensis*. Again, the outer pair may be strikingly branched, as in *A. pulcherrimus* larvæ. The outer pair may be developed into a close tuft or cockade, which is very distinctive, *e.g.* *A. barbirostris*. The two outer hairs behind these may, instead of being very short and inconspicuous, be long and prominent, as in *A. turkhudi*. These different hairs are most helpful in diagnosing species.

The thorax.—Note on the dorsum a short but very strong hair, unlike the others, projecting outwards and forwards. Also a flap-like body may be seen lying at the base of the most anterior hairs on either side. In some Anopheles a fully developed single pair of palmate hairs is found upon the

the breathing tubes from reaching the air and in this way cause death in both the larval and pupal stages. The duration of the existence of larvæ is closely related to the temperature of the water and the amount of food available.

Anopheles pupæ or nymphæ.—(Fig. 26, D.) The pupa is a comma-shaped, very active little animal, which wriggles about in a series of curious jerky movements in the water, coming to the surface constantly to breathe. Pupæ are, however, less energetic than larvæ, and are generally seen floating on the surface. The head and thorax form a large rounded anterior hunch; the abdomen is slender and curled downwards. The thorax is placed on the upper part of the anterior mass and has two trumpet-shaped breathing tubes. The abdomen has nine segments, the ninth being very small, the eighth bearing two relatively large chitinous paddle-like structures. When fully developed they have all the structure of adults. The duration of pupal life is short, in some only forty-eight hours, but it may be ten or twelve days. Temperature greatly affects the period of development. Pupæ are usually brown or greenish in colour; some have a dull reddish hue. Shortly before the imago emerges the

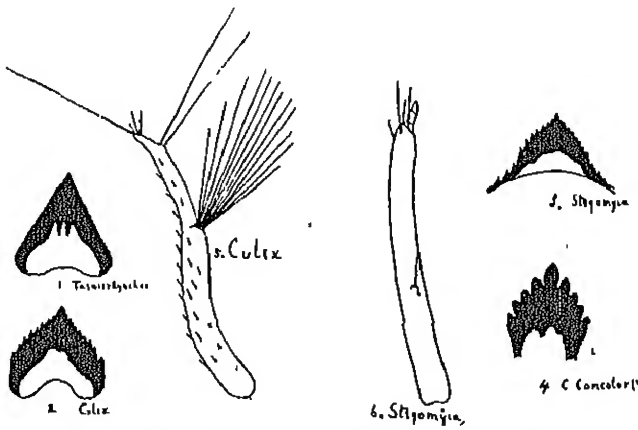


FIG. 29.—Antennæ and mental plates of larvæ.
From STEPHENS and CHRISTOPHERS's *Practical Study of Malaria*, 3rd Ed.

abdomen straightens, the pupal case splits in the median dorsal line of the thorax and the insect gradually extricates itself. The head of the insect appears through the rent followed by the body and appendages, and the imago is set free. After emergence it rests on the pupal case for a few hours to dry and harden its wings, and then flies away.

The stage between the larva and imago lasts about forty-eight hours. When the full-grown larva has cast its larval coat a fourth time the nympha is light in colour and difficult to see. Later it becomes darker, and towards the end and immediately prior to emergence of the imago, *silvery patches* due to collections of air are seen beneath the cuticle.

More detailed description of Anopheles larvæ.—The following structures in Anopheles larvæ require more detailed examination:

The head.—(Fig. 26, B.) Globular and enclosed in a continuous chitinous case. Anteriorly there are the mouth parts; posteriorly there is an opening surrounded by a dark chitinous ring like a collar; the ring has a gap in the middle line posteriorly, and here two diverging bands of chitin form a V on

the notching is very distinct; in *A. stephensi*, *A. maculatus*, *A. theobaldi* and *A. maculipalpis* the filament is a very short and spike-like process (Fig. 32).

The stigmatic syphon.—"The eighth segment bears the stigmatic opening. This is a large quadrilateral space with comb-like chitinous processes on either side. These differ in different species and are of much importance in classification. The ninth segment is cylindrical in shape, and is chiefly notable for the fact that it carries four large transparent papillæ well supplied with air tubes and certain long curved hairs. Of the hairs, one series projects downwards so as to resemble a rudder, the others project posteriorly. There does not appear to be much variation in the different species."[1]

Examination of larvæ and pupæ—accessories required.—Test tubes, watch-glasses, hand-lens, watchmaker's glass, absolute alcohol; methylated spirit, formol, cotton-wool, xylol, Canada balsam, glycerine, glycerine jelly and Farrant's solution.

Larvæ and pupæ should be killed and kept in alcohol (60 per cent.) or formol. For ordinary routine work in India methylated spirit may replace the alcohol. Of formol a 4 per cent. solution (1 part ordinary commercial 40 per

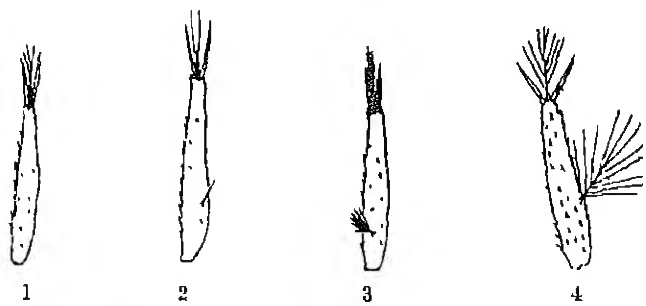


FIG. 33.—Lateral hairs of antennæ of some Anopheles.
1. *A. subpictus*. 2. *A. stephensi*. 3. *A. lindesaii*. 4. *A. hyrcanus nigerrimus*.
From STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed.

cent. solution to 9 parts of water) is strong enough for killing; this preserves them indefinitely and they will be available for microscopical examination at any time. Larvæ and pupæ, whether in alcohol or formol, should be put in small glass tubes and corked, coating the cork with paraffin wax. Put into each tube a scrap of paper on which are written, in pencil or waterproof Indian ink, the locality, date, source, with, if possible, a reference to pinned specimens of the perfect insect, so that these may be identified. They may, of course, if necessary for permanent reference, be mounted on slides with Canada balsam.

Habitats of anopheline larvæ.—They are found chiefly in terrestrial waters. Many species have their own particular habitat but can adapt themselves to other breeding places. The margins of rivers, lakes, pools, ponds, where weeds and grass are found, form favourite spots. They have a special *penchant* for small weakly flowing streamlets where there is an absence of their natural enemies, such as minnows, etc. Runnels of water, water-courses blocked with vegetation, little collections of rain-water on grass, seepage from foot-hills forming marshes, holes and foot and hoof prints and puddles in the soft soil of

[1] STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed., p. 198.

thorax, as in *A. culicifacies*, *A. listonii*, *A. jeyporiensis*; in others it is absent or rudimentary.

The palmate hairs.—These are small fan- or palm-leaf-shaped hairs attached by a short stalk to the outer dorsal portions of certain of the abdominal segments (Fig. 31). Note which segments carry distinct and large palmate hairs and which ill-developed ones. Fully developed hairs occur on all segments of the abdomen (and as stated above on the thorax) in *A. culicifacies*, *A. listonii* and *A. jeyporiensis*. They occur on the second to seventh, or third to seventh, with rudimentary hairs on the second or even first abdominal segment, and on the thorax in *A. stephensi*, *A. maculatus* and *A. theobaldi*. Palmate hairs are limited to the third, fourth, fifth, sixth and seventh segments in *A. barbirostris* and *A. hyrcanus sinensis*; they are confined to the fourth, fifth and sixth segments in *A. turkhudi*.

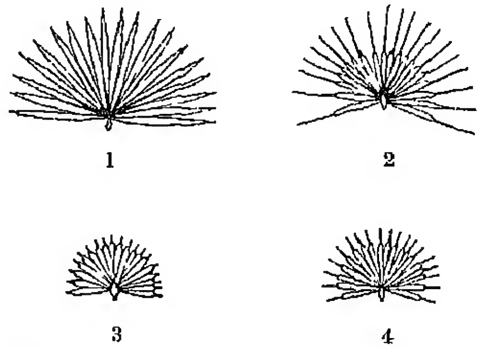


FIG. 31 —*Palmate hairs of some Anopheles larvæ.*
1. *A. nigerrimus*. 2. *A. subpictus*.
3. *A. maculatus*. 4. *A. listonii*.
From STEPHENS and CHRISTOPHERS's *Practical Study of Malaria*, 3rd Ed.

The leaflets.—"In the well-grown larva each palmate hair consists as a rule of nineteen or twenty leaflets, arising close together from a short stalk, and forming (when open) a semi-circular fan. When collapsed, as when the larva is beneath the surface, the hairs are inconspicuous. When, however, the larva takes up its characteristic attitude at the surface of the water, these spread out fan-like and are very striking objects under the microscope."[1] In the fully developed larva there is much variation in the leaflets of different species. In most species they end abruptly in a number of notches or jagged points, the central portion continuing as a filament (Fig. 32, 2–5). The following types of leaflets have been distinguished:

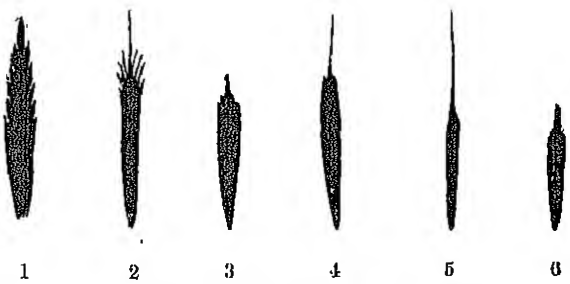


FIG. 32 —Leaflets of palmate hairs
1. *A. hyrcanus sinensis*, *A. barbirostris*. 2. *A. lindesaii*.
3. *A. theobaldi*, *A. stephensi* 4. *A. listonii*, *A. culicifacies*.
5. *A. subpictus*. 6. *A. turkhudi*.
From STEPHENS and CHRISTOPHERS's *Practical Study of Malaria*, 3rd Ed.

One group of unbroken lanceolate shape, having saw-like notches along the edge of the outer half; there is no terminal filament—*A. hyrcanus sinensis* and *A. barbirostris* larvæ (Fig. 32, 1). In another group the filament is long and attenuated—*A. subpictus*, *A. culicifacies*, *A. fuliginosus* and *A. listonii* (Fig. 32, 4, 5). There are some other differences in the leaflets of various species, *e.g.* in *A. subpictus* the filament is as long as the leaflet, and there is no visible notching where the two join; in *A. theobaldi*

[1] STEPHENS and CHRISTOPHERS's *Practical Study of Malaria*, 3rd Ed., p. 196.

similar water containers, empty most of the water and strain the rest through muslin; rinse the chatty or bucket a few times to take up in the rinsing water larvæ that may adhere to the sides and bottom; then empty the contents of the muslin filter into a basin of clean water. Each of these methods —with spoon, mug and net—is applicable in different circumstances. Larvæ in tree-rot holes, in the axils of cocoanut, date and areca palms, banana and papaya trees may be sucked into glass tubes. Put all the larvæ into bottles or specimen tubes. Mark on the glass at once with grease or black pencil the source, and record in the notebook any points of special interest; these notes are essential, as it is not uncommon to investigate a few dozen breeding places in the same day. In the laboratory or work-room separate pupæ and larvæ. Put the pupæ into a jar half full of clean water on which are some grass blades. Tie mosquito netting over the mouth. Place the jar near a window, but not in direct sunlight. Transfer the larvæ to a basin of water, preferably the water they were living in, exposed to direct sunlight. Do not cover. Examine daily for pupæ, and when present put them into the jars. In collecting fill a test tube with mud from the source of the larvæ, another with some form of alga or other vegetation, and some sprigs of grass; put these into the dish or basin containing the larvæ in the laboratory. Each jar and basin should have its own card on which dates of occurrences should be noted—number of larvæ and pupæ, number dying, number bred out, dates, etc. Enter other particulars in notebook for future reference.

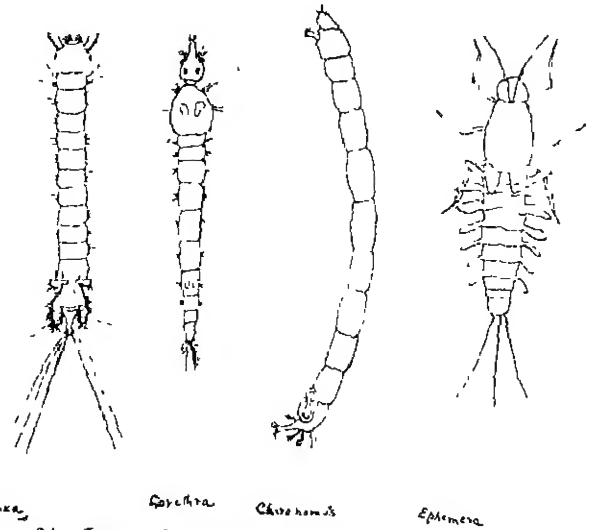


FIG 34.—Larvæ that may be mistaken for mosquito larvæ
From STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed.

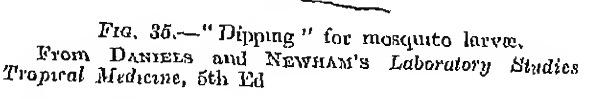


FIG. 35.—"Dipping" for mosquito larvæ.
From DANIELS and NEWHAM'S *Laboratory Studies in Tropical Medicine*, 5th Ed

Examine the larvæ, dividing them into as many groups as possible, noting

boggy marsh land, borrow-pits parallel with railway lines, roadways, especially in the monsoons, and canal embankments, pits used for watering gardens, artificially made collections of water for adorning private and public gardens, excavations in rocks, etc., may all contain them. They thus differ from larvæ of Culex and Stegomyia, which prefer small collections of water in the immediate neighbourhood of houses. Anopheline larvæ prefer marshes (fresh, brackish or salt), or collections of water comparable with marshes. Hence marshes are commonly associated with malaria, from which arose the names of *paludism*, *marsh fever*. Anophelines are in some places known as *marsh mosquitoes*. They are rarely found in rapidly running clear streams. Irrigation canals and channels and rice-fields are favourite breeding places.

When water contains weeds it is difficult to recognise the different kinds of larvæ by the naked eye. Water weeds form favourite cover under which anophelines hide from their natural enemies, especially small fish. Hence pools and shallow lakes containing weeds, which to the naked eye show no larvæ, are often stocked with them.

The collection of mosquito larvæ and pupæ.—The requisites are a metal mug or cup with handle and white enamel lining, white-enamelled metal basin; an ordinary dessert spoon (preferably one with a sharp edge), glass tubing; calico or *mulmul* hand-net, small wide-mouthed clear-glass bottles, specimen tubes or test tubes, notebook, paper, coloured grease pencil, hand-lens. Sometimes there is an advantage in having a cup with a *long* handle, which may be easily improvised, and something in the shape of a cook's ladle is often of service. A small hand-mirror is useful in searching the water in cisterns, barrels and the edges of pools. It is used to reflect the sunlight on the surface of the water where direct sun's rays are absent.

Examine in the dry season all collections of water in the area. Squat near the edge of a stream, pools in the bed of a drying-up river, collections of water in *nullahs*, etc. Watch the surface of the water; unless the larvæ are very plentiful, few will be seen at any one time on the surface. Agitate the water with the spoon or hand; stir up larvæ from the bottom, or get them away from any vegetation present, where they may be under cover, then wait. If present they are readily seen on the surface of muddy water. If none appear stir up again and again, patiently watching for five, or even ten, minutes before considering the search negative. When larvæ are seen dip them out with the spoon and transfer to the mug held in the left hand. Thoroughly scour out the edges. Eddies and backwaters of streams are favourite places. Waters covered with *Lemna major* and *minor* seldom contain anopheline larvæ, nor are they found in quick-flowing currents unobstructed by vegetation. When many have been collected, spoon off or pour off excess of water, and empty the residue contained in the mug into a test tube. A tube can hold about thirty larvæ, and is better than a bottle; being less shaken, fewer larvæ die. If very large numbers are being dealt with, however, bottles are almost indispensable.

In "dipping" for larvæ the mouth of the mug or cup should be turned towards the bank and plunged in, but so inclined that the water at the edge rushes into it (Fig. 35). Then turn the cup straight and remove it. Let it stand for a minute or so until the sand and mud have subsided. Use a hand-lens, as larvæ a day or so old are not easy to see with the naked eye. Do not agitate the water before dipping or the larvæ will go to the bottom.

When using a net, periodically empty its contents into a basin and wash the larvæ into a dish. In collecting larvæ from chatties, fire buckets and

The tarsal bands.—Note whether banding, if present, is in each segment, is apical or basal or both, whether slight or well marked, whether there is any speckling.[1]

The ungues.—Compare those of *A. funestus* and *A. subpictus* (Fig. 13, p. 69).

(x) Nomenclature of Indian Anophelini

Considerable changes have recently taken place in the nomenclature of the Anophelini. The classification here adopted is that of Lt.-Col. S. R. Christophers, C.I.E., O.B.E., F.R.S., I.M.S., Central Research Institute, Kasauli, which is based on widespread examination of type specimens. The Anophelini include one genus only, *Anopheles*, divided by the male genitalia in five sub-genera, of which three, *Anopheles*, *Nyssorhynchus* and *Myzomyia*, are found in and about India. Free use is made of sub-species or varieties.

Examination has shown that many forms, passing under certain names in certain localities, are identical with forms otherwise named in other localities, and, in accordance with the Law of Priority of the Rules of Zoological Nomenclature, the earliest given name is the valid one and has been adopted. For instance, *Anopheles hyrcanus* (Pallas, 1771) was named *Culex hyrcanus* by Pallas in 1771, and is limited to the Mediterranean region. Christophers places it in the sub-genus *Anopheles*, signified by writing it *Anopheles* (*Anopheles*) *hyrcanus*. *Anopheles sinensis* Wiedemann, 1828, he classes as a sub-species of *A. hyrcanus*, and it is accordingly written in full as *Anopheles* (*Anopheles*) *hyrcanus* var. *sinensis*, or *Anopheles* (*Anopheles*) *hyrcanus sinensis*, or the name may for convenience be shortened to *Anopheles hyrcanus sinensis*, or *A. sinensis*. At the same time the form described as *A. jesoensis* Tsuzuky, 1902, having been deemed identical with *A. sinensis*, the latter name is valid, since it holds priority in this case by seventy-four years.

SPECIFIC NAMES OF INDIAN ANOPHELINI AND THEIR SYNONYMS

Correct Names.	Synonyms.
Anopheles (*Myzomyia*) *aconitus* Donitz, 1902	*a birostris* Theobald, 1903. *brahmacharii* Christophers, 1912.
A. (*Anopheles*) *aitkenii* James, 1903	*fragilis* Theobald, 1903. *pallidus* Ludlow, 1905. *treacheri* Leicester, 1908.
A. (A.) *annandalei* Baini Prashad, 1918	*asiaticus* of Christophers, not *asiaticus* Leicester, 1904.
A. (A.) *barbirostris* van der Wulp, 1884	? *vanus* Walker, 1860.
A. (M.) *culicifacies* Giles, 1901	*listonii* (♀) Giles, 1901. *indica* Theobald, 1901. *punjabensis* James, 1911.
A. (M.) *culicifacies adenensis* Christophers, 1924.	
A. (M.) *fuliginosus* Giles, 1900	*leucopus* Donitz, 1901. *jamesii* Liston, 1901. *nagpori* James and Liston, 1904. *freeræ* Banks, 1906. *adiei* James and Liston, 1911.
A. (A.) *gigas* Giles, 1901.	
A. (A.) *gigas simlensis* James, 1911.	
A. (A.) *gigas refutans* Alcock, 1913.	

[1] *Speckling* means the markings on the femora and tibiæ, and in some cases the first tarsal segment.

the main characters of each. Place each group in a small clear-glass bottle, covering its mouth with mosquito netting as soon as larvæ have become nymphæ. When the adult hatches out, note any conspicuous characters before it is removed. It is good practice to get familiar with as many kinds of larvæ as are met with—Chironomus, Ephemera, Libellula, etc. (Fig. 84). Collect specimens of these for more detailed examination in the laboratory.

It is useful to examine fresh specimens of mosquito larvæ of different ages to note the process of feeding. For detailed examination mounted specimens are necessary. Kill the larvæ as above, dehydrate in alcohol, clear in oil of cloves or xylol and mount in Canada balsam. Place strips of cardboard under the cover-glass. Another method is to boil the larva in 10 per cent. potash for a half to one hour, until it is nearly transparent. Wash out all the potash in water. Stain, if required, in saturated alcoholic solution of basic fuchsin. Dehydrate in alcohol, clear in oil of cloves and mount in balsam (R. Newstead). This gives elegant results. In examining fresh larvæ on a slide, do so in a drop of water with a cover-glass, and examine with a ½-, and afterwards with a ⅙-inch objective.

(ix) Recognition of Species of Adult Anopheles

A few hours spent with someone who has acquired the habit of identifying adult Anopheles and collecting their larvæ for demonstration, is more profitable to the uninitiated than weeks of perusal of descriptions and studying plates and diagrams. Having ascertained that the insect is an Anopheles, we endeavour to find out what *species* it is by detailed examination of the costal spots, wing field, wing fringe, cross veins, palpal bands, male genitalia, tarsal bands, ungues, and the characters of the larva and ovum.

The costal spots.—The chief spots on the wing are formed by areas of dark spots in the costal, auxiliary and first longitudinal veins. The spots are, with few exceptions, constant in each species. Variations, however, occur, *e.g.* in the typical T spot of *A. subpictus*, and in the characteristic spot of *A. stephensi*, and they may differ in the right and left wings. Costal spots are, nevertheless, very important in determining species.

The wing field.—The collection of dark scales here also causes a number of minor spots on the veins, *e.g.* the dark areas on the third longitudinal vein in *A. listonii* and *A. culicifacies* are different. Here, again, variations occur in the same species.

The wing fringe.—Where each longitudinal vein meets the costal vein (which passes round the wing) there not uncommonly occurs a light area. Note that the fringes of *A. culicifacies* and *A. listonii* differ from each other (Plates II and VI).

The costal veins.—The position of the supernumerary mid and posterior veins is not of much specific importance, since this factor is very variable.

In some species of Anopheles the wings are so covered with dark scales (*e.g. A. hyrcanus nigerrimus*) that the spots are not very obvious, yet they are literally spotted winged mosquitoes.

The palpal bands.—The palpi consist of four segments. Accumulations of white scales frequently occur at the junction of two adjoining segments, forming a band. Variation occurs in the same species, especially at different seasons of the year, so that in this and other markings, *e.g.* leg bands, species must not be founded on too slight differences.

The male genitalia.—These will give much help in distinguishing species. It will generally be advisable to stain and mount the genital segments.

Correct Names.	Synonyms.
A. (*M.*) *tessellatus* Theobald, 1901	*punctulatus* of James and Liston, and of Mathis and Leger. *deceptor* Donitz, 1902. *thorntonii* Ludlow, 1904. *ceylonica* Newstead and Carter, 1910.
A. (*M.*) *theobaldi* Giles, 1901.	
A. (*M.*) *turkhudi* [1] Liston, 1901.	
A. (*A.*) *umbrosus* Theobald, 1903 . . .	*similis* Strickland, 1917.
A. (*M.*) *vagus* Donitz, 1902	*formosaensis II* Tsuzuky, 1902. *immaculatus* James, 1902. *flava* Swellengrebel, 1917.
A. (*M.*) *willmori* James, 1903	*indica* Theobald, 1907. *dudgeoni* Theobald, 1907. *maculosa* James and Liston, 1911.

(xi) Synoptic Table of Indian Species of Anophelini, Sub-genus Anopheles

(Arranged to include variations of the species)

The following synoptic table, condensed by Lt.-Col. Clayton Lane, I.M.S., for the author from Lt.-Col. Christophers's invaluable work dealing with all Anophelini, will be found useful and convenient.

1. Anterior edge of wing normally with four dark costal spots; no accessory spots in area of sub-costal junction. (Old World) (Sub-genus *Myzomyia*) . . . 14
   Anterior edge of wing with less than four main costal spots; or if four spots are present they are associated with accessory spots in area of sub-costal junction (Sub-genus *Anopheles*) 2
2. Wings have pale spots on costa or field 5
   Wings without pale spots. (Head-scales linear, rod-like) 3
3. Head-scales expanded—of ordinary anopheline type (with striations reaching to base) 4
   Head-scales linear, rod-like . . . . *aitkeni*
4. Knee-spots on hind femora not conspicuous (Europe) . . . *plumbeus*
   Knee-spots on hind femora conspicuous . . . . . *plumbeus barianensis*
5. Femora of hind legs with conspicuous tuft of outstanding scales . *annandalei*
   Femora of hind legs not so 6
6. Conspicuous broad white band on hind femur and about junction of middle with outer third 7
   Hind femur not so marked 8
7. Hind femur pale beneath for some distance; pale spots at ends of veins 3 and 4·2 (Northern India, Japan) . . . . *lindesayi*
   Hind femur dark beneath to coxa; no pale spots at end of veins 3 and 4·2 (Highlands of Southern India) . . . . . . *lindesayi nilgiricus*
8. Costa with basal portion uninterruptedly dark 11
   Basal portion broadly pale with small accessory dark spots 9
9. Apex of female palpi dark 10
   Apex of female palpi pale. (Hills of Ceylon) . . . . . *gigas refulgens*
10. Fringe spots conspicuous. (Highlands of Southern India) . . . . *gigas*
    Fringe spots inconspicuous except the large spot between veins 5 and 6 (Himalayas, Assam, North Burma) . . . . . . *gigas simlensis*
11. Palpi of ♀ with several pale rings 12
    Palpi entirely dark 13

[1] Strictly this name should lapse as a homonym.

Correct Names.	Synonyms
A. (A.) *hyrcanus sinensis* Wiedemann, 1828 .	*sinensis* Wiedemann, 1828. *jesoensis* Tsuzuky, 1902.
A. (A.) *hyrcanus nigerrimus* Giles, 1900 . .	? *nero* Doleschal, 1851. *plumiger* Donitz, 1901. *indiensis* Theobald, 1901. *bentleyi* Bentley, 1902. *minutus* Theobald, 1903.
A. (M.) *jamesii* Theobald, 1901.	
A. (M.) *jeyporiensis* James, 1902.	
A. (M.) *jeyporiensis moghulensis* Christophers, 1924.	
A. (M.) *karwari* James, 1903	*nigerans* Stanton, 1912.
A. (M.) *kochi* Donitz, 1901	*tessellata* of Mathis and Leger. *ocellatus* Theobald, 1901. *flava* Ludlow, 1908. *halli* James, 1910.
A. (M.) *leucosphyrus* Donitz, 1901 . . .	*elegans* James, 1903.
A. (A.) *lindesaii* Giles, 1900	*maculata* Theobald, 1910. *pleccau* Koidzumi, 1924.
A. (A.) *lindesaii nilgiricus* Christophers, 1924.	
A. (M.) *listoni* [1] Liston, 1901	*fluviatilis* James, 1902. *leptomeres* Theobald, 1903. *candidiensis* Koidzumi, 1924.
A. (M.) *ludlowi* Theobald, 1903 . . .	*flavescens* Swellengrebel, 1921. *hatorii* Koidzumi, 1924.
A. (M.) *maculatus* Theobald, 1901 . . .	*pseudowillmori* Theobald, 1910.
A. (M.) *maculatus dravidicus* Christophers, 1924.	
A. (M.) *maculipalpis indiensis* Theobald, 1903 .	*maculipalpis* of James and Liston, 1904. *jamesii* of Stephens and Christophers, 1902. *splendidus* Koidzumi, 1924.
A. (M.) *minimus* Theobald, 1901 . . .	*christophersi* Theobald, 1902. *formosaensis I* Tsuzuky, 1902. *cohæsa* Donitz, 1903. *mangyana* Banks, 1905. *alboapicalis* Theobald, 1901. *flavirostris* Ludlow, 1913. *febrifera* Banks, 1914. *merak* (*cohæsa*) Mangkoewinoto, 1919.
A. (M.) *minimus varuna* Iyengar, 1924.	
A. (M.) *pallidus* Theobald, 1901 . . .	*fowleri* Christophers, 1911.
A. (A.) *plumbeus barianensis* James, 1911.	
A. (M.) *pulcherrimus* Theobald, 1902.	
A. (M.) *stephensi* Liston, 1901	*metaboles* Theobald, 1902. *intermedia* Rothwell, 1907. *folquei* de Nello, 1918.
A. (M.) *subpictus* Grassi, 1899 . . .	*rossii* Giles, 1899. *error* Theobald, 1903. *indefinita* Ludlow, 1904.
A. (M.) *superpictus* Grassi, 1899 . . .	*palestinensis* Theobald, 1908. *nursei* Theobald, 1907. *cardamatesi* Newstead and Carter, 1910 *macedoniensis* Cot and Hovasse, 1917.

[1] This name should strictly lapse as a homonym (= *listoni*) in favour of *fluviatilis*.

Scaling of mesothorax heavier with line of overlapping broad scales at side in front of root of wing, bases of posterior forked cells distinctly nearer base of wing than that of anterior. (Baluchistan and Western India) *jeyporiensis moghulensis*

24. Apical segment of female palpi normally all pale, *i.e.* usually on this account the palpi have three pale bands 25
Apical segment of female palpi normally with a dark band, *i.e.* usually on this account the palpi have four pale bands 36

25. Mesothorax with vestiture of broad scales. Prosternal hairs usually totally absent; tips of hind tarsi usually white (except in *A. stephensi*). No prothoracic tuft 28
Mesothorax with vestiture of hairs or narrow scales, though usually with some narrow scattered broader ones towards sides over fossæ. Prosternal hairs present, tips of hind tarsi dark; tarsi of front legs with apical and basal banding. No prothoracic tuft 26

26. Femora and tibiæ not spotted 27
Femora and tibiæ spotted . . . . *ludlowii*

27. Palpi of female with dark pre-apical band equal to, or nearly equal to, the pale apical area. Larvæ with the outer clypeal hairs at least half the length of the inner. Tibiæ usually with well-marked pale longitudinal streak. Male with broad pale band between segments 3 and 4 of the front tarsus. (Oriental Region) . . . . *subpictus*
Palpi of female with dark pre-apical band half or less the length of the pale apical area. (Oriental Region) . . . . *vagus*

28. Tip of tarsus of hind leg not white. (India, Mesopotamia) . . *stephensi*
Tip of tarsus of hind leg white 29

29. Femora and tibiæ not spotted 30
Femora and tibiæ spotted 31

30. Wing darker; pale interruptions on costa very narrow; sub-costal pale spot bridged on vein 1 by dark; vein 5 extensively dark; basal portion of costa mainly dark. Three tarsal segments continuously white, the joint above this (between first and second tarsal) conspicuously picked out with white Sometimes with dark band at base of second tarsal, leaving two and three-quarters only continuously white. Scaling on dorsal aspect of abdomen confined to two or three segments; no pale scales on ventral surface of abdominal segments; scale tuft on ventral aspect of seventh segment not very prominent. Few or no white scales on mesosternal plate of pleura or on prothoracic lobes. (Oriental Region) . . . *fuliginosus*
Wing lighter; pale interruptions on costa in apical half of wing approaching dark in extent, or at least not especially narrow; vein 5 extensively pale; base of costa pale with small dark accessory spots; sub-costal pale area on costa not bridged on vein 1 by dark. (Peninsular India) . . *pallidus*

31. White portion of tarsus forms a continuous area involving at least two whole segments 32
White portion of tarsus involves continuously only one complete segment . 34

32. Two tarsal segments only completely white. Scaling of abdomen broad, but not confined to last few segments. Front tarsi apically banded only. (Peninsular India) . . . . *theobaldi*
Three tarsal segments completely white 33

33. Palpi of female with one broad apical band and two narrow. Seventh and eighth abdominal segments with conspicuous golden hairs and scales. (Oriental Region) . . . . *jamesii*
Palpi of female with two broad apical bands and one narrow Termination of abdomen not conspicuously golden. (India) . *maculipalpis indiensis*

34. Front tarsal banding broader, apical and basal Pale interruptions on costa more extended. Scaling if present on second abdominal segment narrow. 35
Front tarsal banding narrower, often apical only, pale interruptions on costa

12. Palpi with third band from apex not as broad as apical or sub-apical (Oriental Region) . . . . *hyrcanus sinensis*
Third band of palpi often a mere tache. Wing of a general but varying darkness. Light scales usually yellow and opaque. Sub-costal interruption small to minute, typically comma-shaped, often extending to vein 7. (India, Malaya) *hyrcanus nigerrimus*
13. With a projecting tuft of black scales on ventral aspect of seventh abdominal segment in female. (Oriental Region) . . . . . *barbirostris*
Without such a tuft. Leaflets of phallosome small, lanceolate, smooth. Larva without palmate hairs on any segments. (Malaya) . . *umbrosus*
14. Either femora and tibiæ speckled; or hind tarsi are tipped with white; or front tarsi are broadly banded apically and basally; or there are more than three dark spots on vein 6 24
None of these conditions present 15
15. Accessory sector[1] spot absent, or at most represented by a very slight shortening of the dark area on vein 1 underneath the second main costal dark spot 16
Accessory sector spot developed, either separated from sector spot by a short dark length of vein 1 or confluent with the pale sector area giving rise to distinct shortening of the dark area on vein 1 underlying the second main costal dark spot 17
16. Outer half of costa with the pale areas obviously less extensive than the dark. (India, Burma) . . . . *culicifacies*
Outer half of costa with the pale areas as large as the dark (Aden, Hinterland) . . . . *culicifacies adenensis*
17. Palpi of female with apex pale 18
Palpi of female with apex dark. Larva with palmate hairs on segments 4–6 only. Eggs without floats or frilled margin at end. (India) . . *turkhudi*
18. Mesothorax with vestiture of hairs or very narrow scales except anteriorly; tarsi of hind legs if banded only very narrowly and inconspicuously so. (India, Burma) 19
Mesothorax with vestiture of narrow but definite flat scales; hind tarsi banded, if narrowly very distinctly 22
19. Palpi of female with second pale band from apex narrow or moderately broad only. (India, Burma) . . . . *listonii*
Palpi of female with two broad apical bands 20
20. Proboscis with apical half always flavescent; vein 6 with 3 dark spots; fringe spot at vein 6; vein 3 extensively pale, usually without dark spot towards base. Base of costa showing a pale interruption in about half the individuals. (Oriental Region) . . . . *aconitus*
Proboscis usually dark; general coloration of mosquito darker; vein 6 with 2 dark spots; vein 3 extensively pale, but usually with dark area towards base; no fringe spot at vein 6. (Oriental Region) 21
21. Base of costa with interruption or with indication of such; vein 3 pale in greater part of extent. (North-East India and Oriental Region) . *minimus*
Base of costa without interruption; vein 3 very regularly about two-thirds white. (Eastern Peninsular India) . . . . . . *minimus varuna*
22. Tarsi of hind legs unbanded, or only very indistinctly banded. Pale areas in outer half of costa about equal to dark areas. (Mediterranean, Persia, North-West India, Turkestan) . . . . *superpictus*
Tarsi of hind legs narrowly but very distinctly banded. Pale areas on costa in apical half of wing much less extensive than dark 23
23. Scaling of mesothorax not so dense, hairs only or a few narrow scales at sides in front of root of wing; bases of forked cells with that of posterior not nearer base of wing than anterior. (Eastern India, China) *jeyporiensis*

[1] The accessory sector is the small pale interruption on the first longitudinal where it is dark under the second main costal spot. The accessory sector may be separated or fused with the sector, *i.e.* the pale area on the costa internal to that at the sub-costal junction.

C.I.E., D.S.O., only 1 in 1,246. Other malaria-carriers are: *A. ludlowii* (p. 109), *A. maculatus* (p. 110), *A. umbrosus*[1] (p. 114), *A. minimus*[2] (p. 110), *A. willmori* (p. 113), *A. turkhudi* (p. 113).

It is generally stated that one infected anopheline may, during its comparatively short lifetime, infect several persons and thus disseminate malaria. The records of recent experiments tend to show that there is a limit to their infectivity in captivity; but at the present time it is not possible to state how many persons may be infected by one mosquito in nature. The writer has found young zygotes in the stomach wall at the same time that sporozoites were present in the salivary glands, showing that there probably had been more than one infection of the insect. This is not necessarily the case, however, as it has been shown that if malaria-carriers are bred from larvæ and then infected by a single feed of malarial blood, the stages of the development of the zygotes in the stomach walls differ.

Malarial infection cannot, of course, arise from the bite of anophelines unless the latter have fully developed sporozoites in their salivary glands. The anophelines must themselves have been infected from man with some form of malaria parasite at least a week before, and the atmospheric temperature and other conditions must be suitable. Further, the sexual forms in the human blood must be fully developed at the time of the bite and ready for conjugation, if they are to infect anophelines.

It seems from the evidence we possess that in optimum conditions most Anopheles can be infected in the laboratory, but not to the same degree. In nature we know that some are specially concerned with disseminating malaria. BENTLEY, in Bombay, gathered at the same time from the same houses 837 species of *A. stephensi* and 772 of *A. subpictus*; he examined the stomach wall for oocysts and the salivary glands for sporozoites with the following results:

Species of mosquito	Number dissected.	Percentage with oocysts in mid-gut.	Percentage with sporozoites in the salivary glands.
A. stephensi	837	10	3·5
A. subpictus	772	0	0

Therefore *A. subpictus* had nothing to do with Bombay malaria.

The essentially domesticated Anopheles, like *A. culicifacies*, are incomparably more important in spreading malaria than the shyer ones, such as *A. barbirostris*. In any one area usually a few only are carriers, but there may be as many as three or four vectors. It is possible that any anopheline may occasionally be a vector. Anophelines may in the course of long periods, and after many generations of infection with the sexual forms of human malaria parasites, work out for themselves a racial immunity against this infection; further, such inherited immunity may be quite localised.

Mosquitoes decrease as the distance from their breeding-places increases, and in general terms it may be stated that their number in a locality is in inverse ratio to the square of the distance from breeding-places. Thus, if the numbers $\frac{1}{8}$ mile from a breeding-place be taken as unity, the number at $\frac{1}{4}$ of a mile from the breeding-place would be $\frac{1}{2}$, at $\frac{1}{2}$ a mile $\frac{1}{4}$, at $\frac{3}{4}$ mile $\frac{1}{9}$, at a mile $\frac{1}{16}$, and so on (RONALD ROSS). A small pool near at hand is thus seen to be always a more likely source of infection than a large marsh a mile away. This inversion of the square of the distance from breeding places regulates to some extent the number of mosquitoes in special localities. A thick and dense jungle at some distance from habitations cannot be penetrated by anophelines, so that initially, at least, it is unnecessary to remove it. In some instances such

[1] Incriminated in Burma and Eastern Assam.
[2] Incriminated in Eastern Assam and Khassia and Jantia Hills.

less extended. Scaling heavy and profuse on all abdominal segments and with a patch of broad oval scales on second abdominal segment. (Foot-hills of Himalayas from Assam to Kashmir) . . . . . . *willmori*

35. Scales narrow and confined to last two segments or so except for a few that may be found among the hairs several segments higher. (Oriental Region) . . . . *maculatus*

Scales more conspicuous and broader, very variable in extent, but often extending to second abdominal segment. (Peninsular India) *maculatus dravidicus*

36. Abdomen without lateral scale tufts 37

Abdomen with lateral scale tufts. (Mesopotamia, Turkestan, North-West India) . . . . *pulcherrimus*

37. Palpi of female with narrow and about equal pale bands at apex and joints. (Oriental Region) . . . . *leucosphyrus*

Palpi of female with broad pale bands occupying considerable proportion of length of some of the palpal segments, often with narrow as well as broad bands 38

38. Vein 6 and vein 3 without in either case more than three dark spots . . 39

Vein 6 and vein 3 both with more than three dark spots, or at least vein 3 has many spots . . . . *tessellatus*

39. Female palpi with two broad bands closely followed by a narrow band, and this by a further narrow band more basally situated. No projecting tufts of black scales on ventral aspect of abdominal segments. Wing markings of ordinary Neocellia type. No prothoracic tuft. (Oriental Region) . *karwari*

Female palpi with three broad pale bands followed by a narrower band more basally situated. Ventral surface of abdominal segments with projecting tufts of black scales. Dark areas of wing marks much reduced. Small accessory spot in region of sector spot. Prothoracic tuft present. (Oriental Region) . . . . *kochi*

NAMED VARIETIES OF INDIAN SPECIES OF ANOPHELINI WHICH ARE NOT TRUE GEOGRAPHICAL OR SEASONAL VARIETIES AND ARE SUNK UNDER THE SPECIES

A. culicifacies var. *punjabensis*, James . .	Pigment anomaly.
A. fuliginosus var. *nagpori*, James and Liston	Individual variation.
A. lindsaii var. *maculata*, Theobald . .	Individual variation.
A. maculipalpis var. *indiensis*, Theobald .	Not regarded as distinct type by Edwards.
A. subpictus var. *indefinata*, Ludlow . .	Synonym, see p. 95.
A. willmori var. *maculosa*, James and Liston	Individual variation.

(xii) General Remarks on Malaria-Carrying Anopheles of India

Natural malaria-carrying Anopheles in India and Burma.—It is popularly thought that all Anophelini are human malaria carriers. We have no proof that this is so, and we have proof that so far as India is concerned some of them are not carriers. Up to the present only ten Indian species are known to be natural malaria vectors.

A. culicifacies (p. 103) is the most important natural carrier of malaria in India. The sporozoite rate may vary from 2 to 13 per cent. Then comes *A. listonii* (p. 107) with a sporozoite rate often reaching to 6 per cent. or higher. Next is *A. stephensi* (p. 111); sporozoite rate in Bombay 8·5 to 10 per cent.). Fourth is *A. fuliginosus* (p. 106); the sporozoite rate worked out by Lt.-Col. J. R. Adie, I.M.S., in 1911 was 0·5 per cent., and by Col. A. B. Fry,

Knowledge of specific infectibility under laboratory conditions is most valuable and full of suggestion, yet observation of the facts and conditions of infectivity in nature is of much greater practical use, as in any given area it marks out the species that require control (Lt.-Col. A. ALCOCK). Sir MALCOLM WATSON and SWELLENGREBEL have emphasised this; the former has shown how by indiscriminate clearing of jungle almost harmless anophelines may be replaced by noxious ones; the latter recommends as the primary aim of a malaria survey the discovery of the naturally infected anopheline carriers, and the study of their life-history and bionomics thoroughly, both in the larval and adult stages, so as to concentrate efforts at control wholly on the species that are incontrovertibly connected with the dissemination of local malaria.

The Anopheles which is the best local biological host is not necessarily the one most concerned in carrying malaria in any particular place. It is recorded that in one locality *A. ludlowi* was the optimum host with a sporozoite rate of 17·5, the least effective biologically being *A. sinensis* with a sporozoite rate of only 1·5; yet since the latter outnumbered the former by 125 to 1, 107 specimens of *A. sinensis* were infected to every 10 of *A. ludlowii*, so that the least effective local host was the hygienically important one in the dissemination of the malarias.[1]

SPECIES IN WHICH INFECTION OF THE SALIVARY GLANDS WITH SPOROZOITES HAS BEEN OBSERVED IN NATURE IN INDIA (SEE SYNONYMS OF SPECIES pp. 94–96.)

A. culicifacies Giles .	Also infected experimentally.
A. fuliginosus Giles .	Also infected experimentally.
A. listonii List. . .	Also infected experimentally
A. ludlowii Theo. . .	Transmission effected by the bites of experimentally infected mosquitoes of this species.
A. maculatus Theo . .	Also infected experimentally.
A. minimus Theo. . .	A natural carrier in parts of Assam and in the Eastern Himalayas.
A. subpictus Giles . .	Sporozoites have apparently only once been found in this species, although very large numbers captured in malarious districts have been examined (pp. 100 and 106). Transmission effected by bites of experimentally infected mosquitoes of this species. Is a natural carrier in Dutch East Indies.
A. stephensi List. . .	Also infected experimentally.
A. turkhudi List. . .	Also infected experimentally,
A. umbrosus Theo. . .	A natural carrier in Assam.
A. willmori James . .	Also infected experimentally.

SPECIES FOUND NATURALLY INFECTED BUT IN WHICH INFECTION OF THE GUT WITH OOCYSTS ONLY HAS BEEN OBSERVED OR REGARDING WHICH NO DETAILS HAVE BEEN RECORDED.

A. barbirostris Wulp .	Also infected experimentally.
A. pallidus Chris	
A. superpictus Grassi	Also infected experimentally.
A. sinensis Wied. . .	Transmission effected by experimentally infected mosquitoes of this species.

[1] *The Malarias Recent Studies and Their Bearings*, by Lt.-Col. CLAYTON LANE, I.M.S., in *Trop. Dis Bull*, Vol. 20, No. 10, October, 1923, p. 777.

removal may do harm, as where such jungle separates breeding-places from houses.

Pools and collections of water near houses are very important. If pools are distant from houses, mosquitoes may have to fly from their breeding-places to such houses, and it is fairly well known now that where the breeding-grounds are thus distant, mosquitoes do not appear in large numbers in human dwellings. Pools connected with rivers, irrigation channels, gardens, etc., are favourite breeding-grounds of anophelines. They contain abundance of food in the form of lower flora and fauna, such as algæ, crustaceans, etc. In every case a careful search for every possible kind of water collection is necessary before declaring that larvæ do not exist. The writer has never failed to find larvæ of malaria-carrying anophelines in endemic malarial places during the breeding season. All the greatest investigators of malaria in India assure us that "there is no collection of water, however insignificant, which it is safe to disregard as a possible source of larvæ. There are few places, however dry, where by careful search some unexpected source of water will not be found, and the existence of mosquitoes, otherwise difficult to account for, readily explained" (J. W. W. STEPHENS). The same opinion is expressed by JAMES and LISTON [1] and by RONALD ROSS.[2] When there is an absence of the particular breeding-ground that different species of anophelines would select, they may breed in any collection of water.

Some species of Anopheles are intimately connected with the spread of malaria; some, so far, have not been found to be "carriers." There are places where Anopheles are few but malaria common and *vice versa.* An Anopheles may be a good carrier in one region, a poor carrier in another, and unable to carry malaria at all in a third. The same species of Anopheles in any one place may not be equally susceptible to infection by the three forms of malaria parasites.

Although only ten anophelines have so far been proved to be natural carriers of malaria in India, it would appear to be a sound general rule to consider all anophelines met with as potential carriers of malaria until they are proved not to be so, although our anti-mosquito measures should be limited to the known vectors. It is possible that in exceptional circumstances most anophelines may become malaria-carriers. Many species of anophelines have been experimentally infected with human malaria in India, and it is probable that we have not yet ascertained all the species which are natural carriers.

Caution is called for in declaring that any particular species of Anopheles carries or does not carry malaria in a given locality, and especially in stating that any one species does not carry malaria at all. This can only be proved by experiments and observations by trained workers on the spot. *A. punctipennis* has been repeatedly reported to be incapable of transmitting malaria; this may be so in many places, but it is the dominating vector of malaria in others. In the early days of anopheline investigation it was surmised that *A. subpictus* was an important carrier of malaria; we now know that it is not a natural carrier in India and only so to a limited extent in Java.

So far there is little evidence to indicate that different species of Anopheles carry different species of parasites. In several investigations the writer has found that in places where there was only one species of Anopheles carrying malaria, the victims of their attacks suffered from both malignant tertian and benign tertian. There is, however, much evidence to show differences in the degree of susceptibility of species to the different forms of malarial Plasmodia.

[1] *Anopheline Mosquitoes of India*, p. 48.
[2] *The Prevention of Malaria* and *Mosquito Brigades and How to Organize Them.*

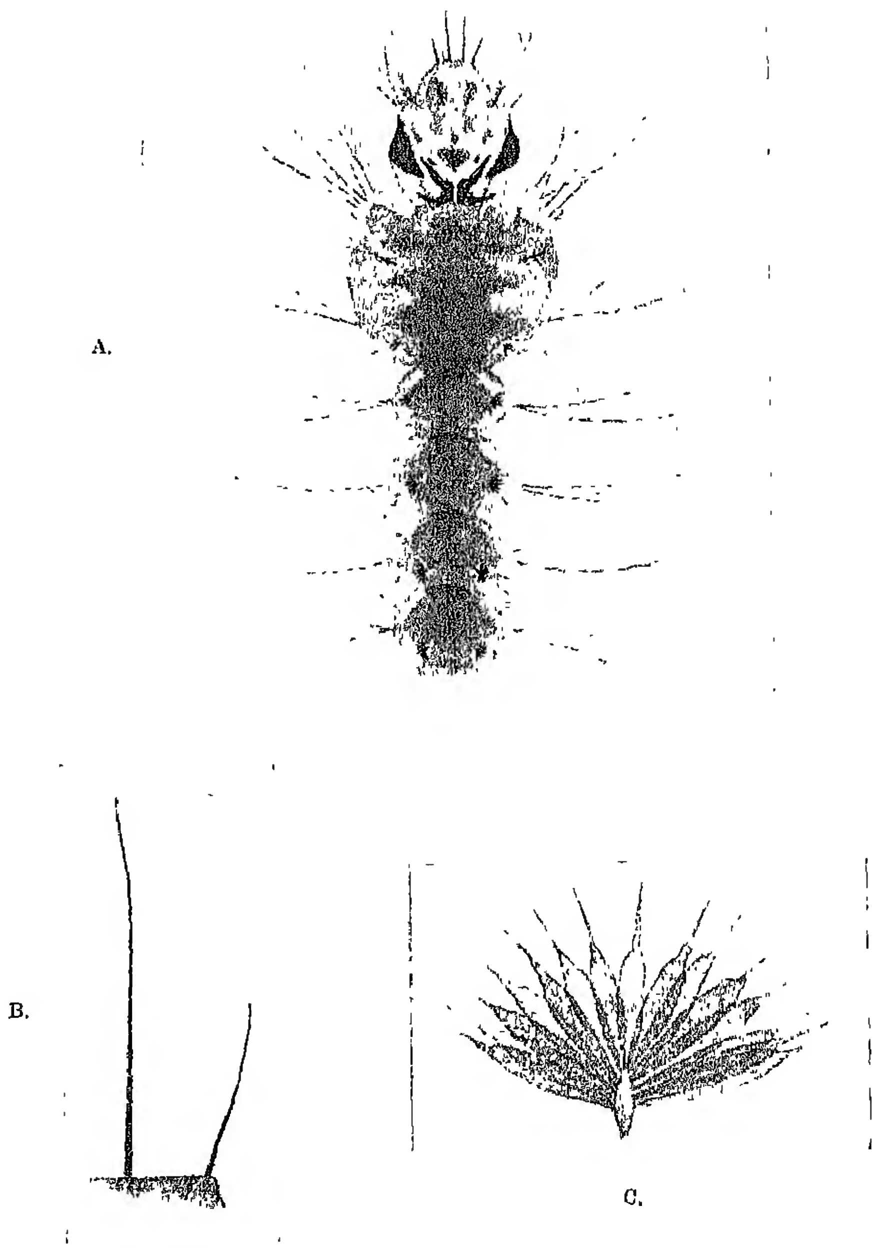


FIG. 36.—The larva of *A. culicifacies*. A. Larva of *A. culicifacies*, general view. B. Frontal hairs of the right side, magnified. C. A palmate hair magnified.

From JAMES and LISTON's *Anopheline Mosquitoes of India*, 2nd Ed.

SPECIES WHICH HAVE NOT BEEN FOUND NATURALLY INFECTED BUT WHICH HAVE PROVED SUSCEPTIBLE TO EXPERIMENTAL INFECTION.

A. karwari James .	. Sporozoites observed in salivary glands.
A. kochi Don. .	. Infection of the gut with oocysts observed.
A. maculipalpis indiensis .	Infection of the gut with oocysts observed.
A. plumbeus Steph.	. Sporozoites observed in salivary glands.
A. punctulatus Don.	. Infection of the gut with oocysts observed.
A. theobaldi Giles .	. Infection of the gut with oocysts observed.

(xiii) DESCRIPTION OF THE MALARIA-CARRYING ANOPHELES OF INDIA

A. (Myzomyia) *culicifacies* GILES, 1901.—(Plate II.) A moderately small dark insect; male lighter-coloured than the female. Wings with yellowish and tawny spots. There are two pale indistinct spots on the fringe opposite the lower branch of the fourth and upper branch of the fifth vein. The third longitudinal vein is black-scaled in its whole length. Palpi slender with three yellow bands, one of which includes the tip. The bands are almost of equal size; the middle band is nearer the terminal than the basal band. The palpi of male are considerably swollen at their ends and the yellowish white banding on them is not conspicuous. Scutum with hairs only. Abdomen dark brown, clothed with yellowish brown hairs, but without scales of any kind. Legs dark brown throughout, but always with a small spot of yellow scales at the apical end of the tibiæ, and occasionally with small spots at some of the other joints. There is *no distinct tarsal banding.* Note the distinct knee-spot of the hind leg. *It rests like a Culex.* The Indian species most resembling it is *A. listonii*, Liston. *A. culicifacies* hibernates as larva.

In nature in the most favourable circumstances the maximum number of *A. culicifacies* found infected was 18·4 per cent. Personally the writer has not found more than 5·3 per cent. infected, and that was at the point of the maximum malaria curve in a severely endemic season in the military cantonment of Delhi in 1909. In captivity as many as 55 per cent. may be infected. This is small compared with the results of some workers on other Anopheles. As many as 100 per cent. of surviving *A. maculipennis* have become infected in the laboratory with a suitable benign tertian case selected for feeding experiments, the air being kept saturated and at a temperature of 22–24° C.[1]

Larva of A. culicifacies.—(Fig. 36, A) The median and external frontal hairs are simple and unbranched (Fig. 36, B); pairs of palmate hairs on the thorax and from the first to the seventh abdominal segments inclusive; the terminal filament (Fig. 36, C.) of each is longer than in the palmate hairs of *A. listonii.* The head pattern is not very characteristic.

Ovum of A. culicifacies.—See OVA OF ANOPHELES, pp. 79–84. Belongs to Type I (see p. 81 and Fig. 25, 1, p. 82).

Distribution.—The whole of India as far south as Madras up to altitudes of 3,000 feet; Assam and Burma. Every station on the plains of India north of the Bombay–Poona–Madras line surveyed by the writer contained this species. Breeds in all kinds of water—in sluggish streams, sheets of fresh rain-water, irrigation channels, rice-fields, collections of water resulting from spring and monsoon showers. It feeds nocturnally. Very prevalent in houses, and is essentially a domestic mosquito. Transmits all species of malaria parasites, naturally and experimentally. It is the chief carrier of malaria in India. "Sporozoite rate in followers' lines Mian Mir, Punjab, 1901, 4·6 per cent., in malarious village Ennur, near Madras, 8·6 per cent." (S. R. CHRISTOPHERS).

[1] S. P. JAMES's "Epidemiological Results of a Laboratory Study of Malaria in England," in *Trans. Roy. Soc. Trop. Med. and Hyg.*, 1926, Vol. XX, p. 143. (See Appendix VI—3, ii.)

A. subpictus[1] GRASSI, 1899 (=*Myzomyia rossii*=*Nyssomyzomyia rossii*)—(Plate III.) "A medium-sized insect which varies from light fawn to dark brown in general colour. Wings light coloured with dark spots. The costa has seven black-scaled areas, three of which at the beginning of the veins are very small, and may be more or less joined together The first longitudinal vein has a small spot near its beginning, and four others beneath the four outer costal spots. The spot beneath the middle costal spot is small, and with the long spots on the costal and sub-costal veins a characteristic T-shaped marking is produced."[2] Palpi slender, with three white bands, the outermost of which is broad and includes the tip; the other two bands are narrow. The second band is much nearer the base than in *A. ludlowii*, so that the dark area between them is longer. In the male the band at the tip is usually divided into two by a narrow black band. Proboscis brown, tip yellow. Thorax and abdomen have hair-like curved scales. Abdomen densely covered with yellowish brown scales, scutum with hairs. The legs are brown and not speckled, broad pale bands on the joints of the front legs. The tarsal joints are banded, but none of the hind tarsal segments are pure white. Is something like *A. ludlowii*, but is easily distinguished from it by the latter having speckled femora and tibiæ.

Distribution.—*A. subpictus* is one of the commonest mosquitoes in India, especially in towns. Occurs practically everywhere on the plains of India and on the lower hill stations. The writer has found it in Bukloh (4,500 feet) and Maymyo (3,900 feet). Its larvæ are frequently seen in rice-fields. On the east and west coasts of India has been found breeding in brackish and even very salt water Is essentially a domestic species, and is not usually found far from human habitations. Is an evening and night biter. Breeds in ponds and temporary dirty pools, puddles, shallow tanks and small collections of water; sometimes in domestic water containers; whereas *A. culicifacies* prefers fresh-water pools, small canals and superficial wells. The inference frequently drawn from the malaria-bearing point of view is that it is not necessary to attack dirty pools and puddles, and that action should be concentrated on the removal of the habitats of ova and larvæ of malaria-bearing Anopheles. The writer agrees that we should destroy the clear collections of water breeding known malaria-carriers first, but we should not ignore the dirty pools and puddles. He has found *A. fuliginosus* and *A. culicifacies* in fairly foul rain-water puddles, and the latter in foul drying-up ponds and pools. (See Appendix VI—2.)

Larva of A. subpictus (Fig. 37).—Both the median and external frontal hairs are simple and unbranched. Palmate hairs are found on the second to the seventh abdominal segments inclusive, rarely on the first abdominal segment, and then only poorly developed; never present on the thorax. The terminal filament of each leaflet is long and attenuated and as long as the leaflet itself, there is scarcely any notching where the filament joins the leaflet. The pattern on the dorsal surface of the head is constant and characteristic. It is the anopheline larva most commonly seen in India.

Ovum of A. subpictus.—(Fig. 25, 3, p. 82.) Belongs to Type II. Has a very broad deck surface and a broad fringe passing all round the edge of that surface.

A. fuliginosus GILES, 1900—(Plate IV.) Wings spotted—chiefly black scaled with minute white spots. Costa has six long black-scaled areas separated by small white spots. The wing fringe is interrupted by white scaled areas opposite all the long veins. Palpi black-scaled with three white bands, the outermost of which includes the tip and is broad; the other two bands are narrow. Proboscis is black with white tip. Abdomen varies from dark brown to black. Last two or three abdominal segments with scales. Legs are black. In the forelegs the distal ends of the femora and tibiæ are tipped with white scales, and at the distal ends of the first, second and third tarsal segments there are white narrow

[1] So far as we know at present *A. subpictus* has nothing to do with the malaria of India. It is introduced here because of its very wide distribution and its specious resemblance to several of the anopheline malaria vectors of that country—*A. ludlowii*, *A. culicifacies*, *A. stephensi*. It has once only been found infected in nature in India, but it can be infected experimentally.

[2] JAMES and LISTON'S *Anopheline Mosquitoes of India*, 2nd Ed., pp. 98–100

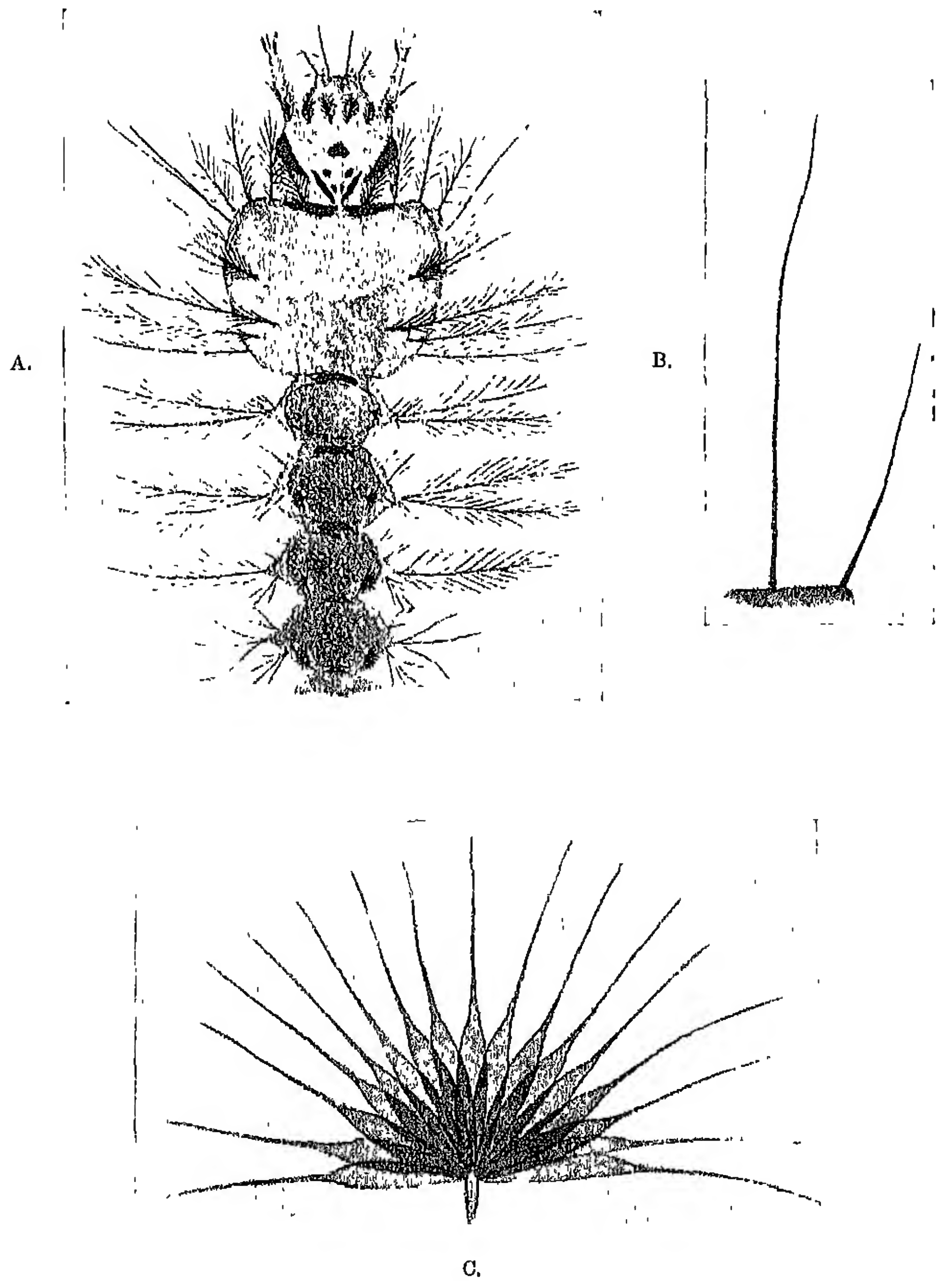


Fig. 37.—The larva of *A. subpictus*. A. General view; B. Frontal hairs right side, magnified; C. A palmate hair magnified.

From James and Liston's *Anopheline Mosquitoes of India*, 2nd Ed.

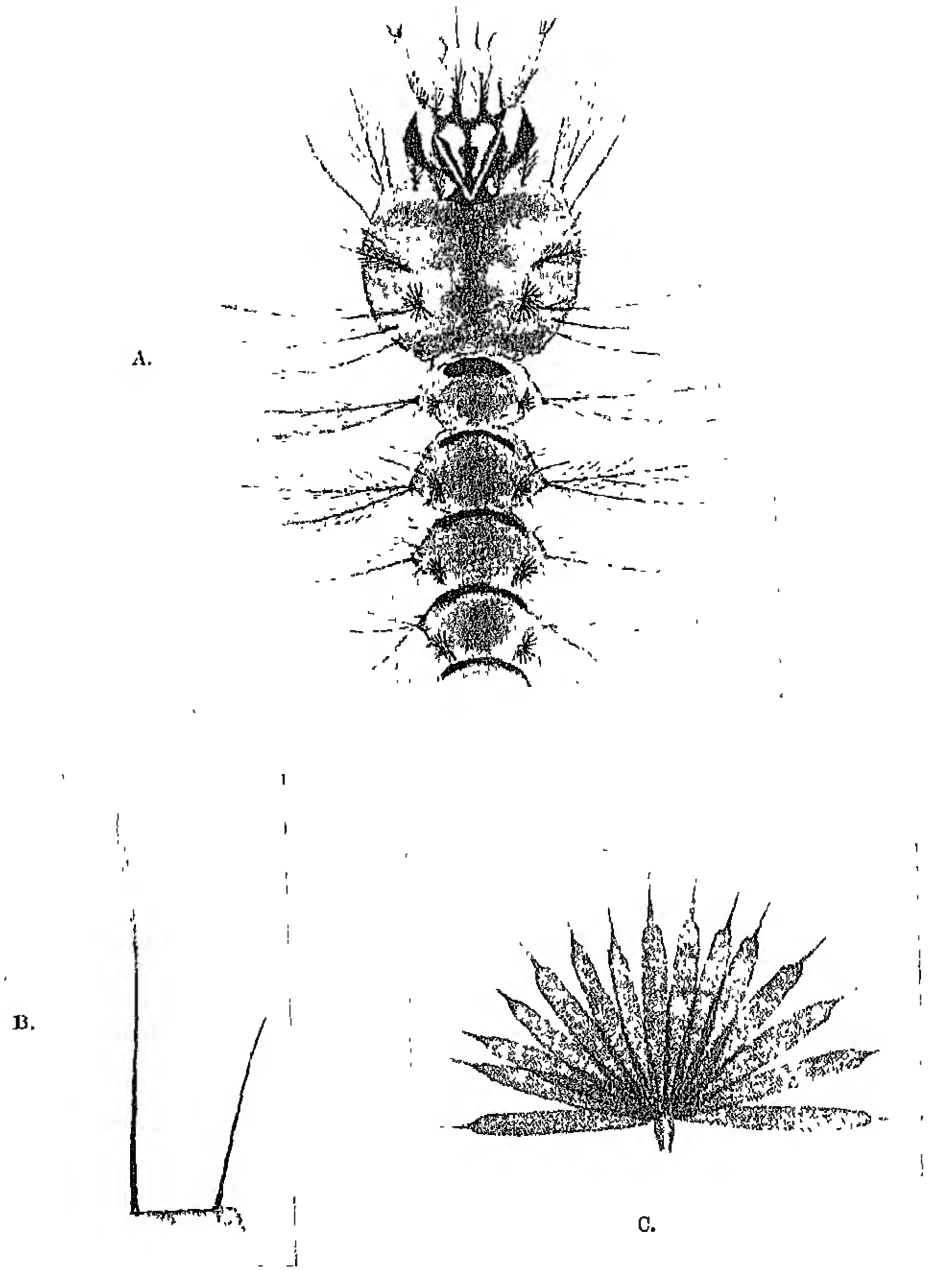


FIG. 38.—Larva of *A. listonii*, Liston. A. Larva of *A. listonii*, general view. B. Frontal hairs of right side, magnified. C. A palmate hair magnified.

From JAMES and LISTON'S *Anopheline Mosquitoes of India*, 2nd Ed.

bands. In the hind legs the distal ends of the femora and tibiæ are tipped with white scales, and the distal end of the first tarsal segment has a narrow white band; the distal end of the second tarsal segment has a broader white band, and half the third (sometimes the whole), fourth and fifth segments are white scaled.

Larva of A. fuliginosus.—The median frontal hairs are slightly branched; branching of the external frontal hairs is well marked; the antennæ are devoid of branching hairs; the palmate hairs extend from the first to the seventh abdominal segment, and there is no pair of palmate hairs on the thorax; the terminal filament of the leaflets is long and attenuated.

Ovum of A. fuliginosus.—See section on OVA OF ANOPHELES, p. 81. Belongs to Type II. (Fig. 25, 2, p. 82.)

The eggs are large and can develop to pupæ and imagines in cold weather when the temperature of the water is 55° F. There is likewise evidence that the eggs can survive for some months in moist earth exposed to frost. Young larvæ have been found in fresh pools in winter in conditions that make it unlikely that the eggs had been deposited there on the appearance of the water. The eggs have no resistance to drying under a tropical sun.

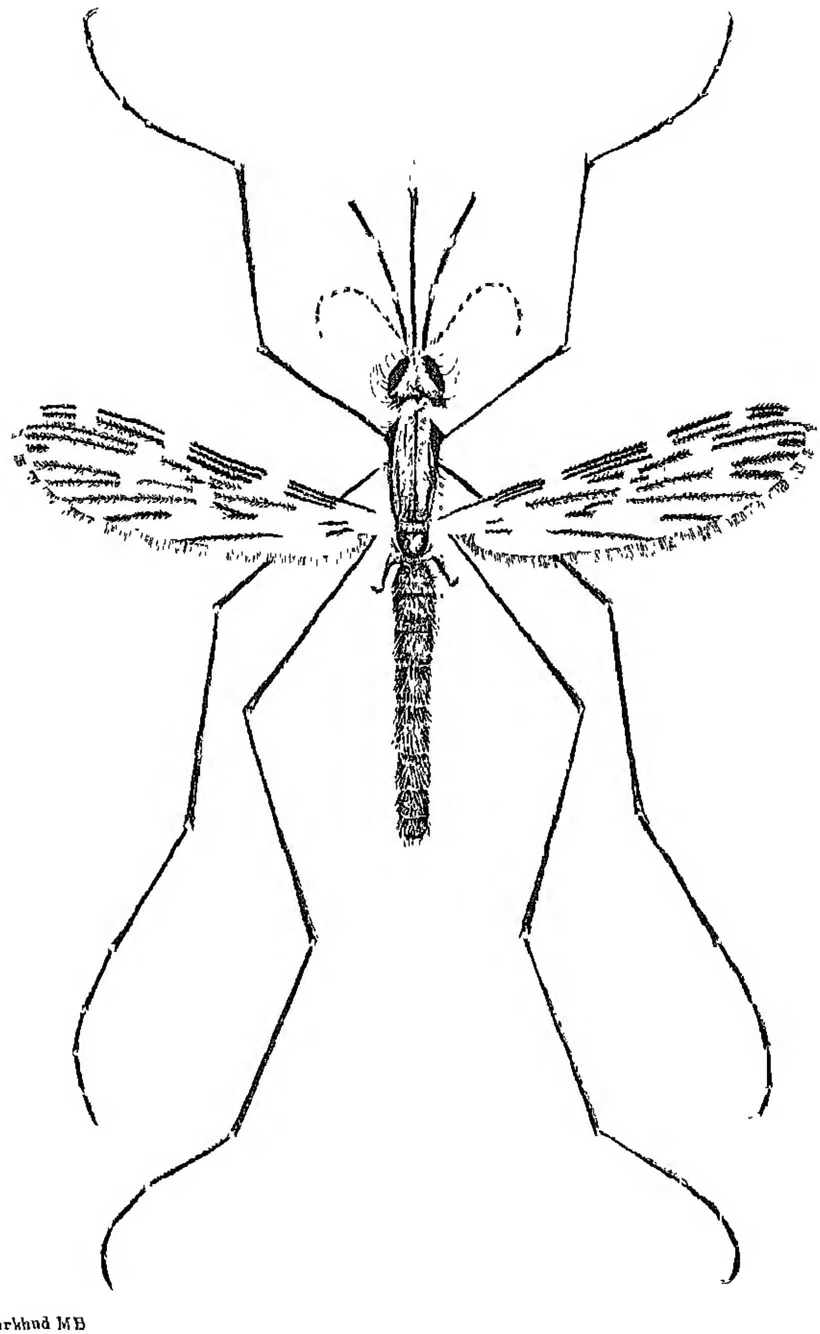
Distribution.—An abundant species distributed throughout India and Burma up to heights of 3,000 feet and over. The writer found this mosquito in tents of convalescent British soldiers at Bhim Tal (5,500 feet), and its larvæ in the lake there in abundance in August, 1909. Usually breeds in swamps, and in tanks, ponds and pools that have grass and weeds at the edges. It is mainly a twilight and night feeder, but attacks at other times. Also *A. fuliginosus* is a house dweller, preferring dark corners of rooms high up out of reach of air currents from doors and windows. Is a strong flier. It is particularly fond of cattle-sheds. Is a natural carrier of all species of malaria parasites, but the sporozoite rate is low. It likewise carries all species of malaria parasites experimentally.

A. listonii LISTON, 1901.—(Plate V.) A small and dark-coloured species. Palpi with three white bands, the third including the tip; the middle band is nearer to the terminal band than the basal band. Wings spotted. Costa has four dark-coloured areas separated by small white spots. This species, though like *A. culicifacies*, is easily diagnosed by its wing characteristics. The first dark area at the base of the costa corresponds in length to the first two dark ones on the costa of *A. culicifacies*, and the fact that it is not divided into two by a white spot forms a good and constant distinction from that species. The third longitudinal vein is white scaled except at its origin and its termination. In *A. culicifacies* this vein is dark scaled almost throughout. The wing fringe is white scaled opposite all the longitudinal veins except the sixth, and very distinctly spotted. In *A. culicifacies* there are only two white patches in addition to that at the apex of the costa. Dorsum of thorax is yellowish brown with a median and two less distinct lateral longitudinal dark lines. Metanotum very dark-coloured with a median darker line. Abdomen nearly black with yellowish white hairs, but without scales of any kind. Legs brown throughout, and nearly always without the little patch of light scales at the apical end of the tibia, which is a constant feature of *A. culicifacies*. *A. listonii* does not rest like a Culex.

Larva of A. listonii.—(Fig. 38, A.) The frontal hairs are simple and unbranched (Fig. 38, B); palmate hairs on all the abdominal segments from the first to the seventh, and a well-developed pair on the thorax, the terminal filament in each being long and thin (Fig. 38, C); the head pattern is often quite characteristic.

Ovum of A. listonii.—See section on OVA OF ANOPHELES, pp. 81, 82. (Fig. 25, 1.) Belongs to Type I. Floats do not touch the rim of the upper surface. Upper surface narrow, separated into two areas, each of which is surrounded by a narrow

PLATE V



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ANOPHELES LISTONII Liston, 1901

From JAMES & LISTON'S Anopheline Mosquitoes of India, 2nd Edition.

Distribution.—Madras, Bengal, Burma and the Andamans. Breeds mainly adjacent to the sea-coast, mostly in brackish water, but also in fresh water all over India. A house visitor. In 1912 S. R. CHRISTOPHERS discovered that it is the natural carrier of malaria in the Andamans, but only operates in a belt round the harbour; villages over half a mile from the coast, even when surrounded by rice-fields or marshes, are free from malaria. The writer visited the Andamans the same year, but later, and found this mosquito to have the habitat defined by Christophers. "Is found in association with *A. umbrosus* in parts of Eastern Assam."[1] "Good drainage clears away the two insects and the malaria produced by them."[2]

A. maculatus THEOBALD, 1901.—Wings spotted. The costa has three very small black spots at its beginning, and then four longer black areas separated by rather long white ones. Palpi black with three white bands, the outermost of which includes the tip. In the male the second white band on each palp is usually divided into two by a narrow black band; it has, therefore, four bands, three broad near the tip, the fourth narrow near the base. Proboscis dark brown with lighter tip. Head thickly clothed with upright forked scales which are very brown at back and sides and white at the top anteriorly. Abdomen dark brown; the first six segments clothed with golden brown hairs, but without scales, the seventh and eighth segments and the genital process clothed with scales as well as hairs. Legs brown. Speckling of legs tawny. The apices of the femora, tibiae and first tarsal segments are tipped with white scales, and at the joints between the second and third, third and fourth, fourth and fifth tarsal segments there are broad white bands, extending equally on both sides of the joints. Only the fifth hind tarsal segment is pure white.

The determination of this species has given rise to a great deal of confusion. Specimens of *A. karwari, A. stephensi, A. willmori* and *A. theobaldi* have been mistaken for it.

Ovum of A. maculatus.—Floats touch the margin of upper surface. Upper surface moderately broad, somewhat contracted where frill ends. Frill narrow, striated, ceases abruptly on reaching the float forming a sharp-turned angle. Floats short, a little more than one-third length of the egg. Lower surface shagreened, unornamented. The egg resembles that of *A. maculipalpis* (Fig. 25, 6, p. 82).

Larva of A. maculatus.—Frontal hairs simple and branched. Palmate hairs present on second to seventh abdominal segments; leaflet moderately long, filament very short.

Distribution.—Occurs in the North-West Himalayas, Northern Himalayas, Khassia and Jantia Hills, South India, Assam and Northern Shan Hills, Burma. The writer found this species breeding in the uncovered reservoirs of the public water supply of Almora (6,000 feet), and captured five female adults in the adjacent dâk bungalow. Breeds in connexion with small mountain streams, in pools in beds of streams, in river-beds near the hills, and in seepage water from land springs; runnels of water in marsh land at foot-hills are a favourite breeding place. It is a natural malaria-carrier, and has been experimentally infected with malignant tertian malaria (STANTON).

Anopheles minimus THEOBALD.—Head dark brown, greyish white in front, scaled as in the *subpictus* group. Palpi with three light bands. Antennæ with base and first two joints scaled; the joints narrow, the first rather longer than the second. Prothorax devoid of scales but with one hair. Abdomen without scales, except on the male genitalia. Legs unbanded. Wings: a large basal spot on the third longitudinal vein, a single apical spot on the sixth longitudinal, and no spot at its termination—which points distinguish it from *A. aconitus*.

[1] SIR MALCOLM WATSON, *Trans. Roy. Soc. Trop. Med. and Hyg.*, 1925. [2] *Ibid.*

frill. Floats long, occupying more than half the length of the eggs, with about twenty crinkles. The egg resembles in general the type of *A. culicifacies*, but the double upper surface is unique.[1]

Distribution.—From North-West Frontier to Central India; West Coast, Assam and Burma. It is a well-known stream and pool breeder. One of the most common anophelines in houses. In moist climates feeds by day as well as by night. Transmits malaria naturally and experimentally: "Sporozoite rate in Duars 6 per cent." (S. R. CHRISTOPHERS). This is the next most frequent carrier of malaria to *A. culicifacies* in India. It is seldom absent in endemic malarial stations.

"Workers in India have found considerable difficulty in differentiating some small specimens of this species from some specimens of *A. culicifacies*, and it would seem in a few places (*e.g.* Bombay) the prevailing variety is *almost exactly intermediate between the two species. In such cases* we are inclined to regard a measurement of the relative length of the first sub-marginal and second posterior cells of the wing as the best test for identification purposes. As a rule it will be found that if the first sub-marginal cell is more than half as long again as the second posterior the specimen is *A. funestus* var. *listonii*, and if the first sub-marginal is less than half as long as the second posterior the specimen is *A. culicifacies*."[2]

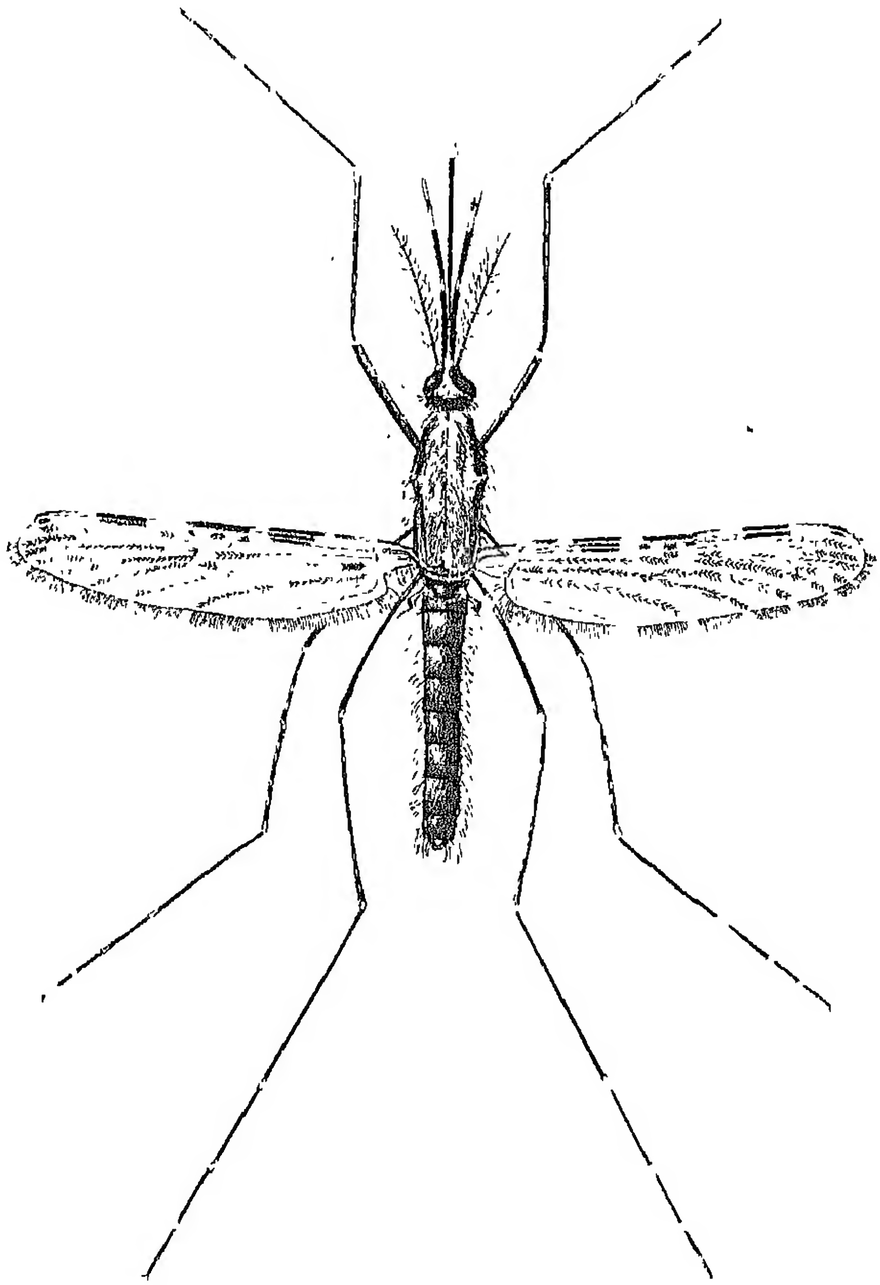
A. ludlowii THEOBALD, 1903.—A medium-sized insect, very much like *A. subpictus*, from which it is distinguished by the speckled femora and tibiæ. "*Palpi* (shorter than those of *A. subpictus*) with three white bands. The outermost band is narrower than in *A. subpictus*, because the last segment of the palp is shorter than in that species. In the *male* insect the palpi have four (sometimes five) distinct broad white bands. *Antennæ* brown, with whitish hairs; in the male the antennæ are very thickly clothed with golden yellow long hairs. *Proboscis* dark brown, with a yellow tip. *Head* with very dark brown upright forked scales at the back and sides, white ones at the top in front. Thorax with dark and light longitudinal areas on the dorsum. Remainder of dorsum clothed like *subpictus*. *Abdomen* clothed with long golden brown hairs, but the last segment and genitalia carry also some rather long white blunt-ended scales. *Wings* like *A. subpictus*, but always with a tiny additional spot on the first longitudinal vein beneath the middle large T-shaped costal black area. Halteres with pale stem and dark knob. *Legs* markedly speckled, as distinguished from *A. subpictus*, with white scales. In the forelegs the femora are only very slightly speckled; the tibiæ and first tarsal segments are much speckled, and at the joints between the first and second, second and third, third and fourth tarsal segments are broad white bands. The bands extend equally on each side of the joint. In the mid legs the femora, tibiæ and first tarsal segment are speckled, and at the joints there are bands similar to those on the forelegs. In the hind legs the femora, tibiæ and first tarsal segments are much speckled, and there are bands at all the tarsal joints."[3]

Ovum of A. ludlowii.—A narrow frill similar to *A. fuliginosus*.

Larva of A. ludlowii.—Anterior internal frontal hairs not so excessively long and filamentous as in *A. subpictus*; the corresponding posterior hairs invariably lie almost directly behind or slightly external to them. They are much finer than in *A. subpictus* and do not reach farther than about the point of origin of the anterior internal hairs. Palmate hairs rudimentary on first abdominal segment; well developed from second to seventh.

[1] *Paludism*, No. 3, July, 1911, p. 60.
[2] JAMES and LISTON'S *Anopheline Mosquitoes of India*, 2nd Ed., p. 75.
[3] *Ibid.*, pp. 102, 103.

PLATE VI



ANOPHELES STEPHENSI Liston
Female
(From BYAM & ARCHIBALD'S Practice of Medicine in the Tropics.)

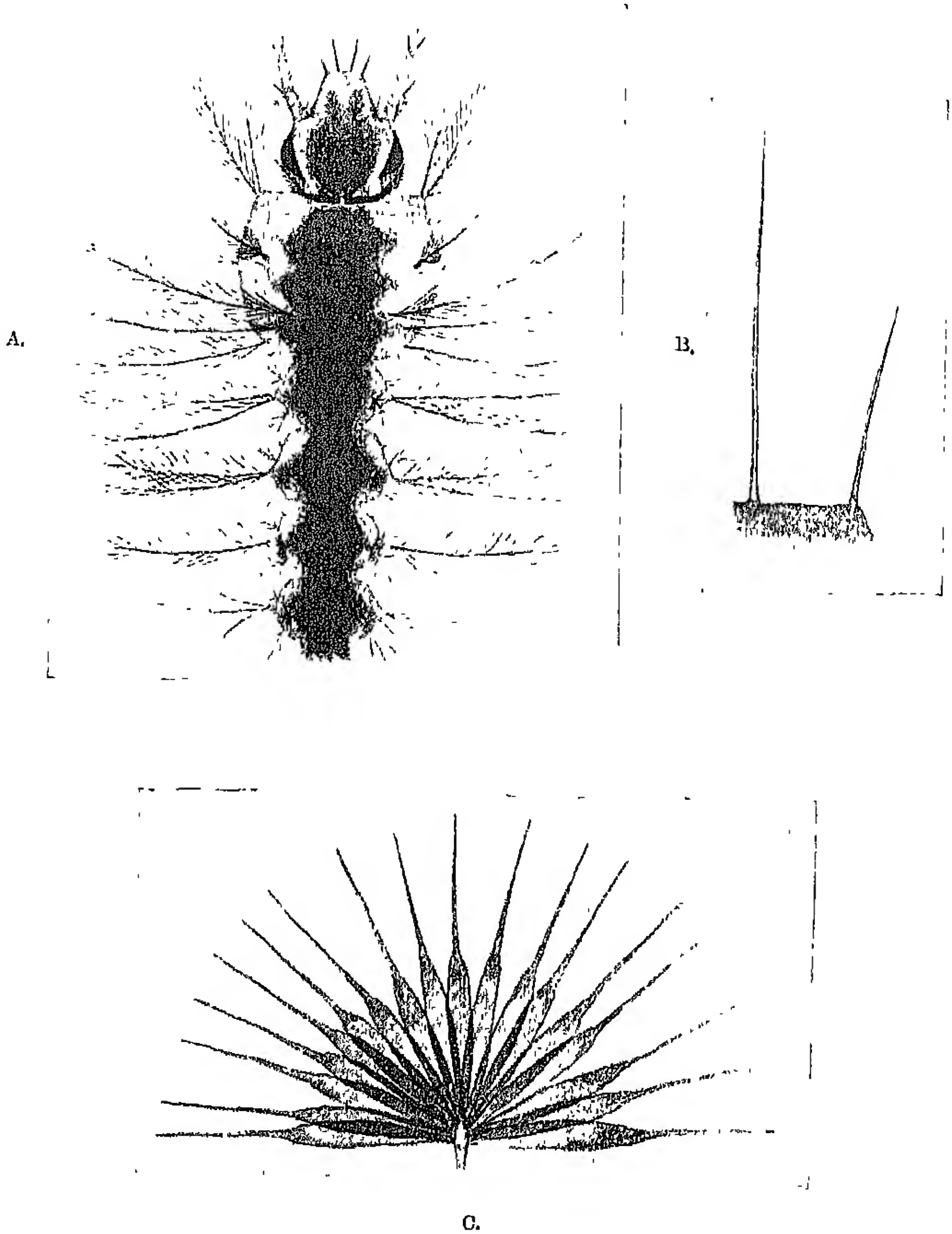


FIG. 39.—The larva of *A. stephensi*. A. General view; B. Frontal hairs; C. A palmate hair.
From JAMES and LISTON'S *Anopheline Mosquitoes of India*, 2nd Ed.

Larva of A. minimus.—3·8 to 4 mm. long. Brownish to greenish grey, with green and violet spots on the thorax. Antennæ without branching hairs. Middle clypeal hairs stout and large, slightly hairy or, exceptionally, smooth. Outer hairs of like character, standing 0·5 to 0·7 mm. from the middle ones. Posterior hairs branched. Palmate hairs on thorax and first to seventh abdominal segments; the filament being about as long as the blade.

Distribution.—In Assam, passing onwards to Malaya, breeding mostly in still water of rice-fields or dead river stretches, more rarely in running water. A dangerous Anopheles.

A. stephensi Liston, 1901.—(Plate VI.) Is a medium-sized insect, generally light brown to dark brown in colour. Wings spotted, and have general appearance of those of *A. subpictus*. "The costa has six black-scaled areas, two being small and near the base of the wing. The first longitudinal vein has four areas corresponding to the outer four on the costa, but the second area (middle of the vein) is only about two-thirds as long as the corresponding costal area and is divided into two unequal parts by a small white spot. The appearance of these markings on the costal, sub-costal and first longitudinal veins has been likened to a T with a full stop *after* it. In *A. ludlowii* the appearance is that of a T without any full stop."[1] Palpi with three white bands with several additional white-scaled patches. The outermost band includes the tip. The next band is near to it and of equal breadth. Then there are some white-scaled patches, above them the very narrow third band, and lastly further white-scaled patches near the base. Scales of scutum yellowish. Abdomen dark brown; dorsal surface of every segment thickly clothed with hairs and rather long yellowish scales. Ventral surface bare of scales except the last segment, which is thickly covered. No scale tufts. In the forelegs the femora, tibiæ and first tarsal segment are speckled with white scales, and there are white bands at the distal ends of the tibiæ and all the tarsal segments except the fourth and fifth. The bands are small and do not extend over the joint. In the hind legs the femora, tibiæ and first tarsal segments are speckled, and there are white tips to the distal ends of the femora, tibiæ and all the tarsal segments except the last. The last tarsal segment is black scaled in its whole length. None of the tarsal segments is wholly white.

Distribution.—An abundant and widely distributed insect, having a superficial resemblance to *A. subpictus*, with which it is often found. Occurs almost universally in India—Indo-Gangetic plain, North-West Frontier, United Provinces, Punjab, Central India, South India, West Coast, Bengal, and also in Burma. Breeds in river-bed pools and backwaters, small artificial collections of water—chatties, fire buckets, domestic water containers, cisterns—and in wells. Is prevalent in houses and a night feeder. Is one of the chief natural carriers of malaria in India; the sporozoite rate has ranged in the same place (Bombay) from 3·5 to 10 per cent. It is the special carrier of malaria in Bombay City. Transmits malaria experimentally very readily.

A. stephensi has a superficial resemblance to *A. subpictus*; they are frequently found together; but in scale characters as well as markings they are very different. *A. stephensi* has also been confused with *A. maculatus*, but its scale structure and general characters are quite distinct from that insect.

Larva of A. stephensi.—(Fig. 39, A.) Both frontal hairs are simple and unbranched (Fig. 39, B); palmate hairs are found from the second to the seventh abdominal segments; an undeveloped pair of palmate hairs is very occasionally found on the first abdominal segment and thorax; the filaments of the leaflets are short

[1] James and Liston's *Anopheline Mosquitoes of India*, 2nd Ed., p. 114.

Ovum of A. willmori.—Of the *A. listonii* type, the upper surface being narrow and divided into two parts. Floats, long with about twenty crinkles, not encroaching on upper surface.

Larva of A. willmori.—There are no distinguishing features to the naked eye. The head has a dark V-shaped mark, with a spot in front of this, and there may be a bar in front of this again and two small spots near the eyes. The antennæ have the usual characters. Spines on antennæ are well developed. Basal hair is branched, and is as long as the antennæ. Frontal hairs simple and unbranched. Two well-developed posterior hairs which reach forward as far as the base of the median hairs. Mental plate bluntly conical; carries nine or ten rounded teeth. Rudimentary palmate hairs on the second abdominal segment; well-developed palmate hairs on third to seventh segments inclusive. Leaflets vary from ten to fifteen in number on the same larva. Leaflets end in three serrations. Short pointed spike-like filament. The spiracle comb has four large processes, one of which carries five teeth.

The larvæ and nymphæ of *A. willmori* are remarkable for their power of remaining at the bottom of the small rocky or stony pools in which they are usually found.[1]

Distribution.—Occurs along the foot-hills of the Himalayas and up to heights of 6,000 feet from the North-West Frontier to Assam. The writer found it in Almorah (6,500 feet) in 1909 in a backwash of running ravine water. Prevalent in the Khassia and Jantia Hills, Chitral and Kangra Valley. Breeds in hill streams. Visits houses and feeds on man. It is a natural malaria-carrier.

A. umbrosus THEOBALD, 1903.—"Head black, with a few upright grey scales in front, black at the sides and behind, narrow white scales between the eyes and a few yellow hairs in front; palpi densely black scaled; antennæ black, basal joint and next few following with black scales.

"Thorax blackish, with traces of linear ornamentation, and golden, hair-like curved scales, and a tuft of median grey ones in front, prothoracic lobes with black upright ones, and also some projecting from the front of the mesonotum; scutellum grey, darker in the middle; mesonotum deep brown.

"Abdomen steely black, with brown hairs.

"Legs testaceous, with brown to almost black scales, the joints with small pale bands, involving both sides of the joints.

"Wings with the costa black, broken by a single small yellow spot at the apex, with a prominent yellow spot at the end of the lower branch of the second long vein, extending up to the third long vein; the small costal spot extends on to the first long vein and partly on to the upper branch of the second long vein; there is a pale spot on the lower branch, remainder of the first and second long veins black, the other veins mostly pale scaled, with a few scattered dark ones and dark spots as follows:—at the base of the third long vein, at the apices and base of the second fork-cell, stem pale, but the basal part of the fourth vein black scaled; fifth long vein with two dark patches on the upper branch, and one large one at the apex of the lower branch and two spots on the sixth; fringe all dark, no pale spots where the lower branch of the fifth joins the costal border; first sub-marginal cell much narrower and longer than the second posterior cell, its base much nearer the base of the wing; cross veins wide apart, the mid more than its own length nearer the base than the supernumerary, the posterior nearer the base than the mid cross-vein; body scales dusky. Halteres pale, with fuscous knob. Length 5 mm.

"Closely related to *barbirostris*, but has only one costal spot, no pale fringe

[1] *Paludism*, No 3, July, 1911, pp. 69, 70

and spike-like (Fig. 32, 3); the antennæ possess a single small unbranched hair; the head pattern is not characteristic.

Ovum of A. stephensi.—(Fig. 25, 4.) Belong to Type II (p. 82).

A. turkhudi LISTON, 1901.—A large greenish-brown mosquito, quite different in appearance from *A. culicifacies*. Palpi with three narrow white bands and brown tip. Wings dusky with yellow spots. Costa has six black areas separated by white spots. The wing fringe has white patches opposite the terminations of all the longitudinal veins except the sixth. Scales of third longitudinal vein mostly dark yellow. Scutum with hairs only. Palpi with three narrow white bands of equal width. Palpi in *male* shorter than proboscis, and the end segments are much swollen. Thorax with hair-like scales. "The thoracic scales of *A. turkhudi* are long, sharp-pointed and curved, and although they are distinctly broader than the scales on *culicifacies* and *listonii*, are quite sufficiently broad for it to be seen at once that they are true scales; they are very narrow in their whole length."[1] Abdomen olive green and clothed with long golden brown and whitish hairs, but without scales of any kind. The legs are very long and dark brown, with a patch of yellow scales at the lower end of the femora and tibiæ and sometimes with very small yellow spots at some of the tarsal joints, but without any distinct tarsal banding. None of the hind tarsal segments are white.

This insect has been described under several names. For discussions on the synonymy see *Ind. Jl. Med. Res.*, Vol. III, No. 1, p. 190; *Bull. Ent. Res.*, Vol. III, p. 249, and Vol. V, p. 133. "Possibly some of the synonymy may require revision, especially as regards the recognition of definite local varieties" (S. R. CHRISTOPHERS).

Larva of A. turkhudi.—"There are no palmate hairs on the first three abdominal segments; for this reason the larva rests on water in a slanting attitude. In addition to two unbranched frontal hairs a third pair of simple hairs (the 'posterior hairs') are long and conspicuous and project over the mouth parts behind and between the frontal hairs."[2]

Ovum of A. turkhudi.—Belong to Type III, p. 82. Peculiar in that the lateral floats are absent or very rudimentary, sometimes quite invisible; the upper surface is rudimentary; frill at one end of deck. (Fig. 25, 5.) The eggs of *A. turkhudi* are massed in ribands.

Distribution.—Occurs on the North-West Frontier, Punjab and Central India; it is indeed fairly widespread in India. Breeds especially in connexion with large sandy river-beds; also found in temporary collections of water near houses. Visits houses sometimes in considerable numbers. Carries malaria experimentally (STEPHENS and CHRISTOPHERS, and S. P. JAMES).

A. willmori JAMES, 1903.—Wings spotted, with the veins clothed with rather broad scales forming black and white spots. Costa has four large and three small black areas, the latter near the base of wing. Markings of wings very characteristic. Palpi black scaled with three white bands, the outermost of which includes the tip. The two outer bands are broad and of equal breadth, the third is narrow. The palpi are not speckled. Proboscis is black with lighter tip. Only the fifth tarsal and the lowest third of the fourth segment are pure white, with spotting of the femora and tibia. Abdomen has dorsal surface of every segment clothed with broad, blunt and round-ended scales, and long hairs with no tufts. The ventral surface of the first six segments is entirely devoid of scales, but on ventral surface of last two segments there are a number of scattered scales.

[1] JAMES and LISTON'S *Anopheline Mosquitoes of India*, 2nd Ed., p. 81. [2] *Ibid.*, p. 80.

band on every abdominal tergum. The coxa and base of femora are pale; legs and proboscis unbanded. The thorax is covered with narrow, curved, golden brown scales; abdomen has basal pale bands to the segments; the legs and proboscis are unbanded. The stem of the first marginal cell is always less than one-fifth the length of the cell. It breeds in fresh water in compounds—in cisterns, rain-water barrels, kerosene oil tins, bottles and miscellaneous artificial water containers of any sort near houses, even in cesspits. It is the commonest and most widely distributed mosquito in India. It can be told by the first sub-marginal cell being immensely long. It transmits filariasis to man, and, in India, is the common carrier of Proteosoma of birds. Is incriminated in the dissemination of dengue in India and Burma, and dog filaria (*Dirofilaria immitis*). It has been observed by J. W. W. STEPHENS that *C. fatigans* fed at night on sparrows that roosted in trees; in the daytime, to avoid the glare, it resorted to a dry culvert in the compound in thousands. It is met throughout the tropics 40° N. and S. of the Equator, having a similar range to Stegomyia. *Culex fatigans* passes the winter as an adult female, which hides in protected places. Breeding goes on up to the beginning of the cold weather.

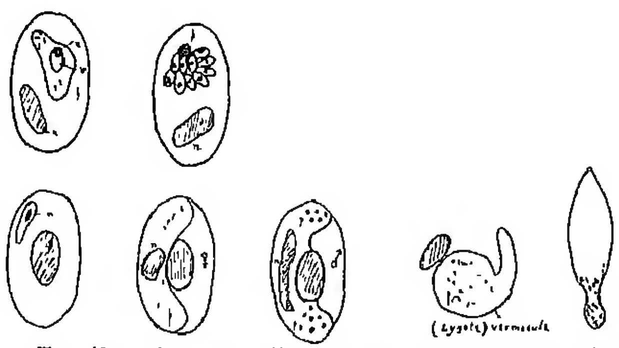


FIG. 40.—(Upper line) Proteosoma, showing medium-size parasite and segmenting form. (Lower line) Halteridium, young form, female and male gametes and vermicule.

From STEPHENS and CHRISTOPHERS's *Practical Study of Malaria*, 3rd Ed.

A high percentage of sparrows is naturally infected with Proteosoma. Tie a small cloth hood over the head of such a bird and bind its legs. Place it in a mosquito-proof box (Fig. 41) and add some female *C. fatigans* which have been reared in the laboratory and have not fed. After they have fed for one or two days catch each mosquito in a separate test tube, or place them all in a prepared jar and keep till ready for dissection (Figs. 18, p. 77, and 19, p. 78) and then release the sparrow. The fed mosquitoes are at once distinguished, as their stomachs are distended with blood.

Attach a small piece of sponge soaked in water to the plug of each tube containing a fed mosquito, and place the test tube in an incubator at 80° F. Inspect them and change the piece of sponge daily until the mosquitoes have digested all the blood, which is shown by the abdomen becoming white. Repeat the feeding and daily inspection. When seven or eight days have elapsed since the beginning of the experiment, kill and dissect insects which have become completely free from blood in the same way as for human malaria parasites. Note the zygotes of Proteosoma, which generally occur in large numbers in the stomach wall, and in which very coarse black pigment is seen (Figs. 40 and 49). Feed some anophelines on Proteosoma sparrows and note that no zygotes are formed. Feed some Tæniorhynchus on Proteosoma sparrows, and again note the negative result.

Feed some *Culex fatigans* upon pigeons containing Halteridium; note the negative result. Sparrows in India contain Halteridium so frequently that

spot, and no white scattered scales at the base of the wings. The veins have also a paler appearance, due to there being fewer dark scales "[1]

Larva of A. umbrosus.—Average length at maturity, 5 mm. Head: anterior clypeal hairs—inner long, simple; outer with few branches as compared with *A.* [*hyrcanus*] *sinensis* and *A. barbirostris*, the stem usually dividing near the base into two or three branches. Posterior clypeal hairs short, branched, with three or four divisions. Occipital hairs short, branched. Antenna carrying on its inner side a long, stout, branched hair.

Thorax: sub-median anterior thoracic hairs as in *A. sinensis*. No stellate tuft.

Abdomen: no stellate tuft on any segment, a unique character, its place taken by a much-branched plumose hair.[2]

A. umbrosus has been found in the Bilapara Frontier Tract, Assam, where the spleen index is 100.[3] The Assamese anopheline fauna follow closely that of Malaya.

The failure or only partial success of anti-malarial work in many localities is sometimes due to non-identification of the particular species of Anopheles which are the local malaria-carriers. There is no doubt that the confused nomenclature of anophelines in the past is partly responsible for this difficulty. We are only too conscious that it is often impossible to destroy all breeding places of anophelines, but if we determine the species acting as essential local vectors, and if these have restricted breeding places, their abolition will effect a material reduction of human infection with the least labour and cost. It should be remarked that even when the main anopheline carrier has been determined it is useless to assume that its larval habitat in any district is necessarily the same as is the case even in an adjoining one. The habitat must be actually determined in every locality for every species. Even then perplexities are not at an end, for a mosquito, when the favourite kind of breeding ground is rendered useless to it, may readily take to another kind, so that a constant watch must be kept with this in view.[4] The writer would emphasise that primarily *only those Anopheles which can be definitely incriminated as carriers of malaria parasites should be attacked*, and that a knowledge of specific larval characters is indispensable in locating breeding places and doing away with them. Many years of anti-malarial effort have been wasted by non-observance of this rule.

(xiv) Study of Avian Malaria in India

Culex fatigans Wied. and Proteosoma in Sparrows

In the study of bird malaria the greatest interest attaches to Proteosoma and Halteridium, especially the former. *Proteosoma grassii* infects a large number of indigenous sparrows; the insect host of this hæmamœbid is *Culex fatigans* Wied., regarding which a few remarks are here introduced.

Culex fatigans Wied.—(Plate VII) It is essentially a domestic mosquito, and is not a strong flier; bites at night, especially indoors, in most districts viciously, and is then the most annoying of all mosquitoes, but in some districts not at all. It is a smallish to medium-sized insect, varying in colour from dark brown to yellow, with a broad whitish or yellowish cross

[1] *A Monograph of the Culicidæ of the World*, Vol. III, p. 87. F. V. Theobald, British Museum (Nat. Hist.), London

[2] A. R Stanton, "Larvæ of Malayan Anopheles," *Bull. Ent. Res.*, Vol. VI, 1916, p. 171.

[3] *Ind. Med. Gaz.*, January, 1924, p 62.

[4] N. H. Swellengrebel and J M. H. Swellengrebel de Graaf, "A Malaria Survey in the Malay Archipelago," *Parasitology*, 1920, September, pp 180–98; review in *Trop. Dis. Bull.*, Vol. 17, No. 2, February 14, 1921, p. 130.

nocturnal, that is, active all through the night. The majority of Indian mosquitoes are nocturnal, their chief biting times are after sundown, during the night, and from dawn to sunrise; these are the times when most malarial infections occur During the day they obscure themselves amongst shrubs and bushes; in dark corners of native huts, tents, houses, stables, cow-byres, out-offices, go-downs; in rafters, almirahs; inside boots. They avoid direct sunlight. Some favour dark objects, dark clothing being particularly attractive. When the sun sets they leave their hiding-places in search of the blood of man and animal. The reproduction of night-like conditions of darkness or shade and stillness in the daytime brings them out of their hiding-places to attack man. The specially domestic kinds, such as *Culex fatigans*, and *Stegomyia fasciata* and *S. asiatica*, are not often seen remote from habitations, but sometimes may be found in jungles. Occasionally some of the wild or sylvan mosquitoes, contrary to their usual habits, may be found in houses, huts and habitations generally.

The writer has repeatedly watched the matutinal exodus of anophelines from houses. The first effort made appears to be to rise to enter trees where these are in the vicinity. In the trees they are lost sight of.

A few species of Anopheles bite during the daytime as well as at night, *e.g.* *A. listonii*, and are therefore more dangerous as regards malaria. BRUCE MAYNE has shown that one infected anopheline can infect as many as five persons with malaria.

Local irritation from mosquito bites.—The bites of some species are painful, of others painless. The irritation is caused by the fluid injected by the mosquito, which Schaudinn considered contained the enzymes of bacteria; this causes congestion of the part and thus admits of a full supply of food to the surface. The insect's saliva is said to prevent coagulation of blood. MACFIE and WARRINGTON YORKE have shown that the saliva does not contain a hæmolysin. The first thing the mosquito does is to insert its proboscis into the skin, the next is to project this poison, which the insect does before drawing blood. Some people living in mosquito-ridden places acquire an immunity to this poison, which does not in them produce any irritation, just as some become immune to the stings of bees. It is well known that some people possess a natural immunity to this poison. The absence of irritation is therefore not a sign of exemption from malarial infection—it may disguise the fact when malarial infection has occurred. We also know that the bite of Anopheles is associated with less discomfort, pain and annoyance than that of either of the other two chief genera of mosquitoes in this country—Culex and Stegomyia. This is of no importance in the ætiological study of malaria.

In some mosquitoes neither sex can penetrate the skin, and do not suck blood, on account of the structure of the proboscis, *e.g.* megarhinines, which are flower feeders. It is in the domesticated and semi-domesticated species that the thirst for blood is most marked; in them oviposition may be greatly delayed if a feed of blood is not obtained. Temperature and atmospheric humidity appear to bear relation to the biting activities, as greater eagerness and persistence are shown by females in their hunt for blood during warm, damp weather.

Flight of anophelines.—Anophelines—the most delicate of the Culicidæ—are weak fliers, seeking shelter in a wind. The distance anophelines can fly is a question not definitely settled. It is said to be generally restricted to half a mile. Accepting this, the extermination of all breeding places within an area of half a mile radius should eliminate malaria. Immigration of mosquitoes from other areas into cantonments and places where anti-malarial

even if the latter is not observed under the microscope, it is difficult to be sure of its absence.[1]

Proteosoma grassii.—(Fig 40, upper line.) The endogenous cycle of *Proteosoma grassii* (*Hæmamœba relicta*, *Plasmodium precox*) may be observed in the blood of infected sparrows in the same way as in human malarial blood. All stages of development up to segmenting forms are met with in the blood simultaneously.

The sexual forms are spherical hyaline bodies which, in stained specimens, have the same general characters which distinguish the human malaria parasite. The whole exogenous cycle up to the development of sporozoites may be followed by dissecting and examining the mid-gut in infected *Culex fatigans* at intervals in the same way as was described for Anopheles infected with the human malaria parasite.

Halteridium—*Hæmamœba danilewski*.—(Fig. 40, lower line.) In India this hæmamœbid occurs widely in columbine birds, a large percentage of pigeons is infected with it, and so are sparrows; the latter often have *Proteosoma grassii* and *Hæmamœba danilewski* in the blood at the same time.

The parasite is known by its curved halter shape, which encloses the nucleus of the red cell without displacing it. Sometimes young forms are seen, but it is not possible to say whether these are asexual or sexual. Segmenting forms corresponding to an asexual cycle have been described by Sir RONALD ROSS and FIELDING OULD. Male and female gametes having much the same characteristics as the gametes of human malaria parasites may also be observed. Sometimes the development up to the stage of vermicule may be seen on the slide.

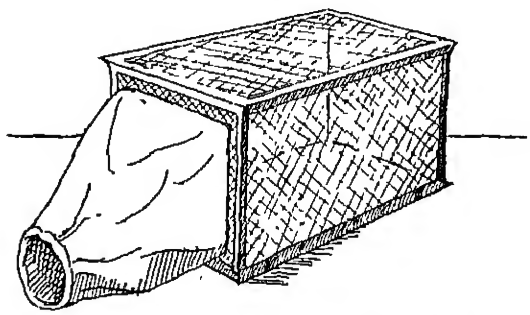


FIG. 41.—Mosquito-proof box for feeding mosquitoes on human malarial blood.

From Lt.-Col. S. P. JAMES's *Malaria at Home and Abroad.*

(xv) BIONOMICS OF MOSQUITOES IN INDIA

Scope of this section.—The biology of the mosquito includes every stage of its life—egg, larva, pupa, adult; its affinities and relation to surroundings. The bionomic relations must include a consideration of its geographical distribution, seasonal influence, habits, range of locomotion, propensity to spread; its food, meteorological influences—temperature, humidity, etc.; fecundity, method of reproduction, breeding places and seasons, duration of life in every stage of its development. Also the relation of the species to its environment, its enemies and parasites and other factors.[2] We have already dealt with some of these in PART I, Section D, and now propose to consider the remainder so far as present-day knowledge permits.

The time at which mosquitoes bite.—Some species are diurnal, some crepuscular, and others nocturnal. There are few, however, that are strictly

[1] STEPHENS and CHRISTOPHERS's *Practical Study of Malaria*, 3rd Ed., p. 250.

[2] Lt.-Col. A. ALCOCK, C.I.E., F.R.S., I.M.S., "Recent Progress in Medical Zoology," in *Trop. Dis. Bull.*, 1921, p. 1.

that of spraying limited breeding places, such as artificial pool traps, tree holes, etc., with carmine and endeavouring to capture the hatched-out adults; this is not an over-successful way. 4. It has been investigated also by spraying with carbol-fuchsin and flour (2 to 1) tree holes in which they harboured. Dipping mosquitoes from these holes into glycerine, alcohol and chloroform (8 : 8 : 1) gives a flash of red.[1] In any circumstance it is extremely difficult to ascertain the distance a mosquito can fly.

Migrations of Anopheles.—In some places there are sudden invasions of Anopheles; huge migrations from outside take place. They arrive, scatter in various parts of the new habitat and gradually settle down in their new home, some of them domesticating. There may be only one flight or the migration may continue for a week or more. Everyone remarks on the sudden accession of mosquitoes. The causes of mosquito migrations are not known, but in all probability they are related to necessities for food supply, reproduction or overcrowding. Intense breeding over large areas may be associated with wide distribution of Anopheles. The activity of winged Anopheles is affected by several external factors, such as atmospheric temperature and moisture, winds and light. The long flights usually occur in a slow-moving warm, moist wind, especially a few weeks after the beginning of the monsoons. All fly against, seldom across, the wind. If it blows hard they either fly low down or go off at right angles to the direction they were following, until they can right themselves again or obtain shelter.

Dissemination of mosquitoes by gradual infiltration.—This is a most important factor in India. It is now well known that the young adults do not always go to the "home" of their parents; not infrequently they go in the opposite direction, or at right angles, and having discovered a suitable place to "live" in and feed, go farther afield for breeding places. In this roaming they may travel some distance, from, say, one village to another, but this is exceptional. Adults may, of course, be transported long distances, by accident and not from choice, in railway carriages, in boats, barges and steamers on rivers and along the coast. Eggs, larvæ and nymphæ may be flushed out of one breeding place to another, and are being constantly transferred in running water.

Factors influencing dissemination of malaria by Anopheles.—Among *the factors which influence the dissemination of malaria by Anopheles are*—species, geographical distribution, numerical prevalence, habits, circumstances which promote or retard the development of the parasite in the insect, length of life, rate of multiplication, distance of flight, nature of ordinary food supply, kinds of water they breed in and the form in which they hibernate and æstivate.

Food of mosquitoes.—The majority of mosquitoes never taste man's blood, and but comparatively few take vertebrate blood. Certain species are, however, natural blood-suckers, especially the Aëdes, and certain species of Culex and Anopheles. Feeding on blood favours ovulation in some species. Most mosquitoes feed on vegetable juices, males do so almost exclusively. They are very partial to ripe bananas; and sliced bananas are one of the best foods to keep them alive. They will also feed on ripe apples, dates, jams, syrups. Many mosquitoes take the blood of mammals, birds and invertebrate animals. Precipitin tests of blood contained in anophelines have shown that certain species prefer bovine to human blood. It is curious that certain species which suck man's blood in some parts of the world do not do so in others. It is the female alone that sucks blood—the males are vegetarians. The recorded instances in which males have been seen biting and sucking blood are

[1] A. L. Hoops, *Monthly Bull. of the Eastern Bureau, League of Nations, Health Section*, 1925, April 20, p. 23, *Trop. Dis. Bull.*, October, 1925, p. 808.

operations continue has been urged against such measures. There is evidence to show that such importation in endemic malarial areas is constantly in progress, but under normal circumstances immigration and emigration balance one another, so that this factor alone should not affect the question of anti-mosquito measures. In an investigation of the malaria in a large division the writer found both winged anophelines and their larvæ in every plains station within half a mile of cantonments, and in most stations in the heart of the cantonments themselves.

Odd trees, shrubs, scattered houses and so forth are no barriers to mosquitoes, but the insects seem not to be able to penetrate a densely populated town—they remain on the outskirts. The only malaria-carrier that seems to thrive in the interior of densely populated towns and cities is *A. stephensi*; it is able to do this on account of its propensity to breed in wells, household water cisterns and other artificial water containers. Anopheles usually fly against the wind. In connection with sites for new buildings and camps it is always better to increase the area to the leeward side from the breeding places rather than to the windward side.

So far as evidence and the writer's observations go, it would appear that as a rule Anopheles do not travel more than about half a mile if unassisted. He has on three occasions on the plains, in cantonments, proved that the morning flight may reach half a mile, as no breeding places existed within this distance. When helped by gentle winds, however, they have been known to travel over a mile. In the Panama Canal Zone ZETEK observed daily flights of hordes of *A. albimanus*; the flights began at dusk, lasted from thirty-five to forty-five minutes, and extended over distances up to 6,000 feet, the return flights to the breeding places being made in the early morning. It has been observed that ships at anchor half a mile from land have been invaded by mosquitoes that have been captured, stained and set free from the shore, and recaptured on the ships. Usually, however, their flight is less than a quarter of a mile; often even much less than this (see p. 181 *et seq.*).

The most important problem is not, how far Anopheles can fly, but how far can natural malaria-bearing Anopheles carry malaria? It does not materially affect the question that in exceptional circumstances Anopheles can fly or be carried by wind for a mile or even several miles, but it is of vital importance to know how far natural carriers can fly in sufficient numbers to maintain malaria as an endemic disease in a locality.

Sir MALCOLM WATSON had this point investigated in the Malay States. It was ascertained that "on flat land the spleen rates were found to fall progressively the farther the children were from the jungle home of *A. umbrosus*, until, at a distance of half a mile, the spleen rates were *nil*. The number of malaria-carrying Anopheles that would travel beyond half a mile is not, then, likely to keep up even moderate endemicity. To the malarial sanitarian it is a question of endemic, that is local, malaria, and not one as to the distance anophelines can fly. Malaria is a local disease in so far that it is maintained by local anopheline vectors of the disease—the anophelines of the next village or town take no part in its diffusion except during periods of epidemic and hyper-endemic malaria (see pp. 49-51 and 181–183).

Methods of ascertaining the distance of flight of mosquitoes.—1. Catching, staining and releasing of mosquitoes, and then recapturing them. This involves a risk of injury that must necessarily affect their flying capacities over long distances. 2. It is possible that by ascertaining the presence of a particular species of Anopheles at different distances from breeding places, all the latter being known, gives more satisfactory results. 3. Another method is

way of destroying hibernating adult anophelines; it is probable that a far cheaper and easier method of achieving this will be discovered than the expensive and laborious measures of destruction used against Anopheles adult and larval in the summer and autumn. Incidentally it may be remarked that Miss NELLY EVANS observed in Calcutta that *Culex fatigans* produces five batches of rafts in the course of its life when fed regularly with blood.[1] During the breeding season each succeeding generation of mosquitoes becomes considerably larger in numbers than the preceding one, and when we consider the rapidity of their multiplication and that this is in geometrical progression, there is obviously an enormous advantage gained in lessening the number of generations.

Hibernation and æstivation of Anopheles.—The method of hibernation and æstivation of malaria-carrying anophelines is of great importance to the tropical sanitarian, for with a knowledge of these he will be able to attack them at the more vulnerable periods of their existence. Hibernation of anophelines is considered to be carried out in the adult stage chiefly in out-houses, under bridges, in the sheltered parts of old ruins, on the under surface of shelves in walls, etc. They may sometimes be seen in masses on inner walls of neglected and empty outhouses.

In India adult female Anopheles may be found, by those familiar with their haunts, at all seasons of the year, the species generally being maintained by the survival of fecundated females, who, during the periods that are unpropitious to the growth and development of larvæ, hide and remain quiescent in secluded dark and sheltered corners, chimneys, nooks and out-of-the-way places, where they are not likely to be found by their enemies, often creeping into cracks and corners which appear too narrow for the admission of so delicate an insect. In thatched houses hibernation has been found to occur in the hollow stalks of individual straws—as many as sixteen Anopheles have been found within a single straw.

When hibernating, mosquitoes are very sluggish, torpid and quiescent, but except in very cold weather they can still fly when capture is threatened. In India such hibernation is probably confined to the north. It is doubtful if anophelines hibernate anywhere south of Agra, and in Central India and the Deccan they are in evidence all the year round (GILES). A warm day during cold weather may bring them out and a return of cold sends them back. At Lansdowne (5,500 feet), on November 28, 1909, while writing in a room in which a fire was burning (it was the first fire used that cold weather), the writer was surprised to find several *Stegomyia calopus* buzzing around, as they had not been seen in the station for over a month. The external atmospheric temperature was 40° F., and the temperature of the room at the time of the observation 70° F. The dormant insects were brought out from their hiding-places by the heat of the room. In May, 1915, both at Basra and Kurna (Mesopotamia) the writer found *A. pulcherrimus* æstivating in countless numbers in chimneys; they were resting several deep from apex to grate. A *bhoosa* (dried grass) fire in each grate stupefied them with the smoke and they fell and were consumed. When this is being done the upper opening of the chimney should be closed with gunny or other stuff.

The sensitiveness of mosquitoes to meteorological changes varies, some being hardy, others delicate; thus *C. fatigans* Wied. and *C. impellens* Walk. are fairly active in Northern India throughout the year (GILES). Extra heat and dryness operate on mosquitoes similarly, hence we find that in the Punjab and the United Provinces, after a brief reappearance of anophelines in spring, they once more disappear and remain hidden during the severe heat of May

[1] Lt.-Col. A. ALCOCK's *Entomology for Medical Officers*, 2nd Ed., p. 60.

supposed to be cases of hermaphrodism. The statement often put forward that male Aedes do not enter human dwellings is incorrect—one has seen numbers of them in houses in Delhi, Meerut and Fatehgarh in September. It is certain that anophelines may breed in vast colonies 150 miles away from human beings. It is not necessary that the female should feed on either human or vertebrate blood before laying eggs—*A. maculipennis*, *A. bifurcatus* and *C. pipiens*, kept artificially without blood, will deposit fertile ova. "Mosquitoes breed mainly without the stimulus of human blood" (THEOBALD).

EULING[1] states that anopheline gluttony is such that the female fills herself with five times her own weight of blood, and as she prefers her meals in several courses, served generally by different persons, the chances of malarial dissemination are correspondingly increased. Usually the anopheline female feeds on blood and lays eggs two or three days after the feed. Often she dies after depositing her eggs if she has not had another meal of blood during the previous night. The female takes two or three minutes to gorge herself with blood. If watched during this time it will be noticed that at first a droplet of clear fluid is ejected from the anus, then blood-tinged fluid, and finally, what appears to be pure blood is discharged. Anophelines are not hungry for twelve to twenty-four hours after being hatched out or after laying eggs.

Anopheline larvæ are mainly surface feeders and are frequently found where there is an algal scum and Protozoa are present at the surface. Many other mosquito larvæ feed on organic particles at the bottom, some live on the remains of other insects or their exuviæ floating on the surface; many large forms are predacious and cannibalistic. One species of mosquito larva pushes its siphon into the air tubes of aquatic plants to get its oxygen.

Fecundation of mosquitoes.—In nature this occurs soon after escape of the imago from its pupal case. It is, in fact, seldom that an unimpregnated female is found. Pairing occurs in the sunshine. Males collect in swarms and may be seen near ponds and pools, 5 to 10 feet above the surface. One or more females arrive in the swarm, and each leaves in company with one of the males. More females arrive and other pairs are formed. There is obviously much competition for the ladies' favour as there seems to be a good deal of fighting going on. Next the female separates from the male and seeks a place to live in safety while eggs are maturing. This search may result in the female flying some distance. Her choice is determined by finding a safe place in which to lay eggs, and another in which she can get feeds of blood. Her flights are connected with these two functions, with rests in some quiet, sheltered places in the intervals. It is probable that she adheres to the place selected originally as her abode.[2]

Our knowledge as to the method of copulation in many species is still unknown, though it has been observed in some. Union of the sexes may also occur in captivity when bred out from larvæ and placed in test tubes. Eggs have been laid in captivity by females that have never paired, but such eggs do not yield larvæ.

Rate of multiplication of mosquitoes.—Mosquitoes are rapid breeders. All the species of anophelines known in India pass through two or more generations during the period from the commencement of the rains to the setting in of the cold weather.

In one calculation it is stated that each female anopheline which survives the winter produces during the ensuing breeding season 7½ million descendants, a very strong reason for making every possible endeavour to ascertain the best

[1] *Trop. Dis. Bull.*, Vol. 19, August, 1922, p. 571.
[2] S. P. JAMES, *Malaria at Home and Abroad*, p. 68.

61st day; while in a third the corresponding figures were 71 and 66. Sporozoites of *P. falciparum*, apparently dead, were found as late as the 95th day, and of *P. vivax* on the 105th day.[1]

Question of continuance of malarial infection in Anopheles during hibernation.—ROUBAUD, in France, infected Anopheles with crescents in August and found in the salivary glands, early in January, only a few sporozoites, mostly in a state of degeneration. MITZMAIN, in N. America, exposed infected anophelines to winter temperature and found that, even when they were restored to the warmth of the laboratory, the infection was not consummated to the sporozoite stage, even at the end of seventy days. WENYON (1915–19), however, in Macedonia, using *A. superpictus*, observed that the development of oocysts could be arrested for as long as three weeks by cold and then revived by appropriate warmth. MAYER (1920) infected Culex with *Proteosoma grassii* in the autumn and found, five weeks later, that not only the insects' salivary glands but also all the muscles of the body, appendages and palpi were filled with sporozoites, and that even fifty-two days after the infective feed isolated sporozoites could be detected in the muscles. MÜHLENS (1921), also in the autumn, infected Anopheles with *P. vivax*, and in twenty-one and twenty-six days afterwards found the same heavy generalised sporozoite infection in the insects; the ovaries were not infected, although surrounded by sporozoites. The above conflicting observations apply to temperate climates. It is very desirable that the problem of over-wintering of parasites in anopheline malaria vectors should be worked out in India (see pp. 23–25).

Seasonal prevalence of Anopheles.—There is a marked seasonal prevalence of all mosquitoes, including Anopheles, varying with the species. We are as yet not familiar with the way in which various conditions and surroundings affect this seasonal factor. Anophelism, one of the periodical scourges of India, requires special conditions of atmospheric temperature and humidity and the existence of water favourable for breeding (see EPIDEMIC MALARIA, p. 49 *et seq.*).

Numerical prevalence of Anopheles.—It is very desirable to estimate the numbers of Anopheles, especially the malaria vectors, but it is extremely difficult to do this with anything like accuracy. We should remember, however, that the numerical prevalence of anophelines is only one of many factors which influence the spread of malaria, and, in certain circumstances, it may not be the important factor. The amount of malaria in a locality will vary in accordance with the number of Anopheles only when all the other factors remain equal and constant.

Observation stations should be selected, established and visited regularly and the number of adults taken in a definite time in definite conditions counted periodically. Perhaps the best method is the use of mosquito traps.

Traps for adult mosquitoes. — The writer, who had fifteen years' experience in the use of box traps, knows of none that can compare in efficiency for captures on a small scale with that devised by Professor T. BAINBRIDGE FLETCHER.

The ordinary box trap for mosquitoes suffers from the defect (1) that it is not possible to see what is in the box; (2) that it is necessary to use chloroform or benzene to kill the mosquitoes, and the smell of this persists in the box and repels the insects. The new design, which is free from these objections, "consists essentially of a wooden skeleton of a box with a hinged lid covered over on all sides with black mosquito netting. This skeleton box is contained inside an open-topped wooden box which is painted black on the inside. The whole is then placed in a suitable position overnight, and left with the hinged top of

[1] BRUCE MAYNE quoted by CLAYTON LANE in *Trop. Dis. Bull.*, 1922, p. 868.

and June. Most of the *Stegomyia*, *Panoplites*, and other species associated with the rainy season, occur for several months only, and remain hidden during extremes of weather.[1] It is probable that many die during these periods. They are favoured by moderate heat, abundance of water for larvæ and lots of food. Temperature has a great deal to do with the life of the mosquito—the laying of eggs, hatching, development of larvæ and other processes being retarded by cold and accelerated by warmth (see p. 81).

Some Anopheles in India breed throughout the winter, especially in the southern coastal districts. Others, *e.g. A. culicifacies*, hibernate in the larval stage; others, again, hibernate in the egg stage.

The writer has often in India bred out Anopheles from eggs contained in the surface mud of drying ponds and the lateral pools of streamlets that were drying up. In 1904, in Manipur, from local experience, he arrived at the conclusion that certain anophelines hibernated in the egg stage in moist earth. JAMES and LISTON consider that most Indian Anopheles either manage to breed throughout the season or (*e.g A. culicifacies*) hibernate as larvæ.

It is necessary that special observations be carried on to determine the places of hibernation of larvæ, possible hibernation of adults, extent to which æstivation occurs, and the places in which anophelines obscure themselves in the very hot months of summer and during the cold of winter.

Length of life of mosquitoes.—Generally, in captivity, mosquitoes after a time become weak and are often seen to fall into the water when depositing eggs. They find difficulty in hanging on to smooth glass. Even when a rough surface is provided, they are repeatedly found at the bottom of the cage resting horizontally. After depositing eggs they often die the same night. Males are shorter lived than females; many die within six weeks.

In very hot parts of India during summer anophelines which remain through the very dry summer appear to show some peculiarities in their "habits":

(1) "They feed regularly and are found full of blood," thus contrasting with hibernating mosquitoes.

(2) The ovaries are in the majority large and the ova fully developed.

(3) They do not lay their eggs even when test pools are made near the houses in which they abound."[2]

MAYNE has shown that *A. punctipennis*, laboratory bred, fed on dates and water, and kept at a temperature between 45° and 75° F., may live for 231 days. The ordinary period was about three months. For some species the average life in captivity is not longer than six weeks (ALCOCK). Apart from such protection from natural enemies and inclement meteorological conditions, they can live in huts for one or two months or possibly longer.

Duration of life of malaria-infected Anopheles.—*The average duration of life of a malaria-infected Anopheles* has not yet been settled. The point is important endemiologically. The following observation on the survival and viability of malaria parasites in *A. punctipennis* is very interesting. One of these insects was fed upon a crescent carrier. A volunteer host was bitten fifty-five days later, and in due course developed sub-tertian malaria, demonstrated microscopically. On the 67th day this mosquito failed to cause infection in another volunteer on which she fed, although on the 68th day dissection showed very active sporozoites in the salivary glands. A second mosquito was found to harbour living sporozoites on the 70th day, after failing to infect on the

[1] Lt.-Col. G. GILES, I.M.S., *Gnats or Mosquitoes*, 2nd Ed

[2] STEPHENS and CHRISTOPHERS's *Practical Study of Malaria*, 3rd Ed., p. 184.

attractive and cool resting-place. About half an hour after completing the disturbance of vegetation and the smoking of surrounding buildings the door of the trap is closed. Then the imprisoned insects are caught one by one in test tubes (the trap being large enough for a boy to enter) or are simply killed by placing the trap in strong sunlight for an hour or two, by which time all the mosquitoes will be found lying dead on its floor. In a trap of this kind placed in a garden in Colombo there were caught on an average 280 mosquitoes each day for a month during November and December 1918.[1] The whole arrangement is most ingenious. Lt.-Col. S. P. JAMES states: "From experiments with these traps I surmised that if every householder in Colombo could be induced to use such a trap correctly almost 10 million mosquitoes might be caught daily, and that this would be more effective than the daily destruction of 1,000 million larvæ"[2] A gauze trap which acts on the principle of a fish trap may also be used as a snare, and several of the forms used for house flies may be successfully adapted for mosquitoes. They may be placed on the windward side of the house, below the eaves, and in dark corners of rooms.

Regarding the general numerical prevalence, we usually employ such terms as "swarming," "abundant," "scanty," "impossible to detect by search." It constantly happens that of five or six species of Anopheles present in a cantonment or town, only one or two are concerned with the dissemination of malaria.

When practically all breeding-places have been done away with, Anopheles seek other less apparent, possibly inaccessible, places to lay eggs in. In such cases the use of trap breeding-places in various parts of the area under investigation is indicated. "Collections of water in vessels or artificial pools of the kind chosen by the particular mosquito being dealt with should be used as traps and they should be regularly examined for larvæ."

When our means of measuring the actual prevalence of Anopheles has become more accurate, reliable and scientific it will be possible to prepare a chart giving the Anopheles Curve in a locality during any period of days, months or years, and we may then be able definitely to correlate reduction of Anopheles with particular anti-mosquito measures within the insects' range of flight.

Geographical distribution of Anophelini in India.—The geographical distribution of the malaria-carrying anophelines of India is detailed under the description of the individual species, pp. 108–115.

Breeding-places of mosquitoes.—Mosquitoes may be looked upon as forming colonies adjacent to their breeding and feeding grounds. "The vast majority remain close to where they were born." Comparatively few migrate thence. In normal circumstances the immigration and emigration of mosquitoes may be assumed to be equal, except in highly endemic areas, and during intensely malarial seasons in such areas, when the former in all probability exceeds the latter, because the conditions for their rapid multiplication are in existence in such areas and at such times. It may be assumed also that mosquitoes decrease in numbers the further the distance from their breeding-grounds, and whilst the actual ratio of such decrease cannot be estimated by any known mathematical formulæ, the fact that anophelines are naturally weak fliers supports such a supposition.

In every endemic malarial district where malaria has been investigated by experts, there anophelines have been found, and this after their absence has been repeatedly asserted. It is often forgotten that anophelines, though naturally

[1] Lt.-Col. S. P. JAMES, *Malaria at Home and Abroad*, pp. 70, 71
[2] *Ibid.*

the inner box open. In the morning, when the mosquitoes have settled down, the hinged lid is closed and fastened with the metal hook fasteners and the inner box can then be lifted out by the handles provided for this purpose. To kill the mosquitoes the inside gauze box is withdrawn and put in the sunlight; usually in a few minutes the mosquitoes are dead, and even in damp weather they do not survive many hours. The writer recommends that the inside of the box should be black, unless further experiment should discover a colour more attractive." [1]

Lt.-Col. S. P. James, I.M.S., while in Ceylon in 1918, devised a portable trap in which large captures of adult mosquitoes were made. A rough estimate

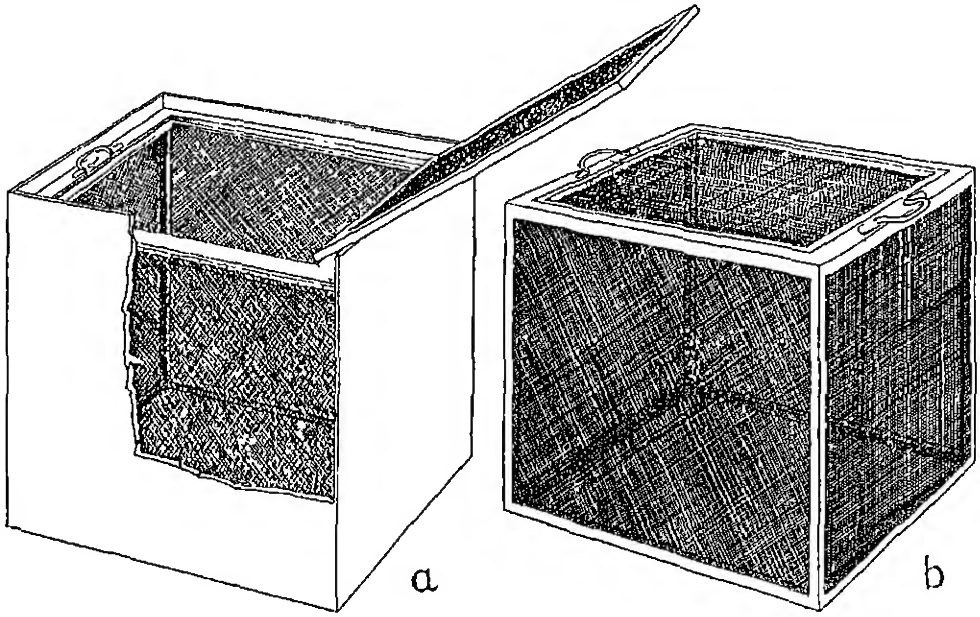


Fig. 42.—Mosquito trap, (*a*) open, and (*b*) closed and removed from outer case. Devised by T. Bainbridge Fletcher.
(Reproduced from *Report of Proceedings of the 4th Entomological Meeting, Pusa.*)

of the numbers caught at different times is an indication of the success or otherwise of the anti-mosquito measures in operation. The trap consists of a rectangular wood framework 5 feet long, 3 feet deep and 3 feet broad, covered with mosquito netting, one end being a door on hinges. The trap is placed on the ground in a shaded corner of a garden, and covered with sacking and a thick tarpaulin so that the interior may be cool and dark. Two or three pots of plants are placed inside each trap, and several near the door, which is left partly open. The trap is set overnight. In the morning, about eight or nine, the vegetation in the vicinity is disturbed as much as possible and straw and paper torches are burnt in the surrounding outhouses and buildings so as to drive the mosquitoes into the open air. The result is that most of the insects quickly find their way into the trap, which appears to them to be a very

[1] *Trop. Dis. Bull.*, March 31, 1923, Sanit. Supplt. No. 1, p. 8.

with hydrants and water-supply taps in military cantonments, swarming with *A. culicifacies* and *A. subpictus* larvæ. The greatest masses of larvæ of malaria-carrying Anopheles have always been found in some moderate-sized pools. Of two similar, fairly adjacent tanks one may, for some unknown reason, contain many anopheline larvæ and the other none. In the Shahjehanpur Cantonment in September, 1909, the author found two circular *singhara* ponds, each roughly 15 yards in diameter, both partly covered with *Lemna*. They were old borrow-pits created during the original building of the barracks. They were identical in every appreciable respect, and were separated from each other by 12 yards. Both contained small fish (unidentified). In one the larvæ of *A. culicifacies, A. subpictus, A. jamesii* and *A. barbirostris* flourished; in the other he could find no mosquito larvæ of any kind.

Hydrogen-ion concentration of water in relation to breeding of mosquitoes.—A vast number of observations has now been made on this subject, and so far as can be judged, with little practical result. It has been stated recently, however, that *A. quadrimaculatus, A. crucians* and *A. punctipennis* have their preferences regarding the degree of stillness and the pH and plankton content of waters. This may be deserving of investigation in connection with the Anopheles vectors of India.

In the matter of breeding-places many Anopheles are selective to an astonishing degree (pp. 320, 330). It is seldom we can recognise the special peculiarity of the collection of water chosen. There appears to be "something in the water" (Sir MALCOLM WATSON); or "some quality of the water strongly affects the distribution, either directly or indirectly, by influencing the character of the food of the larva."[1] There is a possibility of discovering some biological method of control over dangerous Anopheles by influencing and altering the character of the water in which their larvæ thrive. Such alteration may, indeed, be brought about by altering the gross and obvious environment, as when larvæ of *A. umbrosus* disappear as their pools are deprived of shade; or by effecting some change in the composition of the water or of its alga-flora by subtler methods, as when the larvæ of *A. maculatus* are observed to disappear with the spread of a felted alga that flourishes in water that is fouled in certain ways.[2] We will deal later with other Indian Anophelini having a restricted choice of breeding-places.

Mosquito-breeding in cocoanut palms.—The discovery by the late Dr. W. E. HAWORTH[3] of mosquitoes breeding in cocoanut palm trees in East Africa is profoundly interesting. Dr. HAWORTH was M.O.H. for the district and town of Tanga, Tanganyika Territory, in June, 1920, when he made this remarkable discovery. The breeding took place in the crown of the tree in water that collects between the axils and the stems of the leaves. An expert climber collected the larvæ in a bottle, sucking them up a tube formed of the hollow leaf-stalk of the paw-paw tree, which has a diameter of 8 mm. No fewer than twenty-seven species of mosquito were found breeding in the palm water, including two species of Anopheles, eleven species of Aedes, and a large number of Culex of various species. A graphic account of the discovery is contained in an editorial article in *The Lancet* of February 21, 1925.

It is probable that a like state of affairs has existed for thousands of years

[1] W. A. LAMBOURN, *Some Problems of the Breeding Places of the Anophelines of Malaya. A Contribution to their Solution* Abst in *Trop. Dis. Bull*, Vol. 19, No. 16, 1922, p. 831.

[2] Abstract by Lt.-Col. A ALCOCK, C I E, F R S., in *Trop. Dis. Bull*, 1922, p 831

[3] *Mosquitoes and Cocoanut Palms.* A Mosquito Survey of the Palm Trees in East Africa and the Problems Resulting Therefrom By W. E. Haworth, M B., C.M, B.Sc, *Trans Roy. Soc. Trop. Med and Hyg*, October, 1924, Vol. XVIII, No. 4, pp. 162–98

A. ludlowii is a prolific pool breeder. Tufts of grass, bits of stick and every sort of obstruction give shelter to the larvæ.

A. karwari is also a pool breeder, liking specially a quiet stream of fresh water to flow through its pool. Ideal pools for it and for *A. maculatus* are found at the foot-hills. Streams in ravines obstructed by weeds which steady the flow are likewise selected; in this case removal of the grass and weeds causes the insect to disappear; the current overwhelms it. Like *A. ludlowii* and *A. turkhudi*, it also breeds in brackish and even salt water.

The writer has never found anopheline larvæ in large irrigation canals and their branches when these were in *pukka* conduits free from grass and weed;

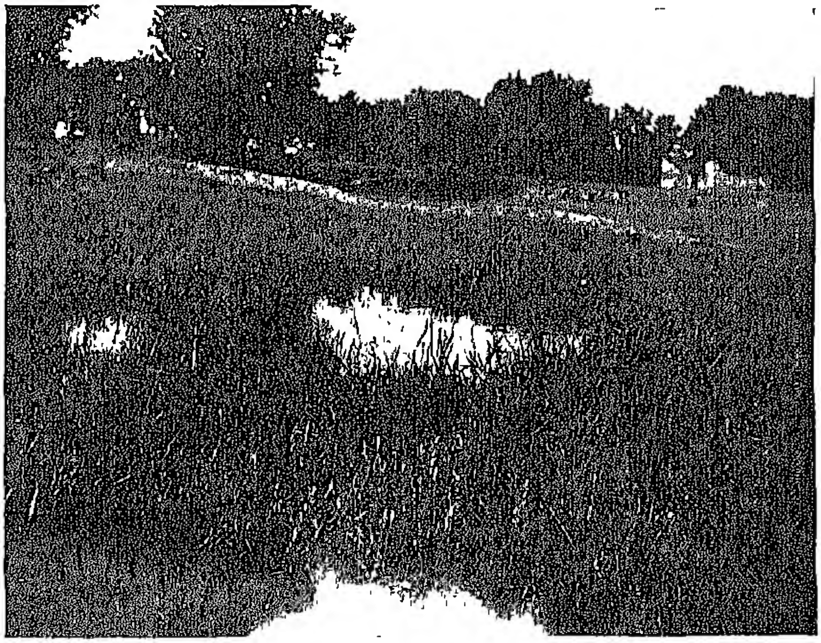


FIG. 44.—Other breeding-pools in the Bareilly Cantonment, August 7, 1900. The predominating species found here was *A. listonii*. They are permanent deep ponds with shelving margins, suitable for clearing and larva-eating fish or vertical drainage (pp. 356, 357).

they were, however, always found in *katcha* irrigation channels, and in the *katcha* waste channels from *pukka* irrigation canals. The absence of larvæ from *pukka* canals is explained by the periodical shutting off of the water or by the rapid flow in a channel usually devoid of grass and vegetation. Anopheline larvæ are specially found under cover of grass and weeds and are not often seen in the open, except in stagnant waters. There are three exceptions to this—*A. subpictus* may be found in deep dirty pools in which buffaloes wallow, and in which there is an entire absence of grass or any other cover, and *A. barbirostris* and *A. nigerrimus* may very rarely be found in small- and medium-sized clear pools without grass or weeds. The smaller and moderate-sized collections of water are more favoured by anophelines for oviposition than the larger. The writer has often found comparatively shallow pools, connected

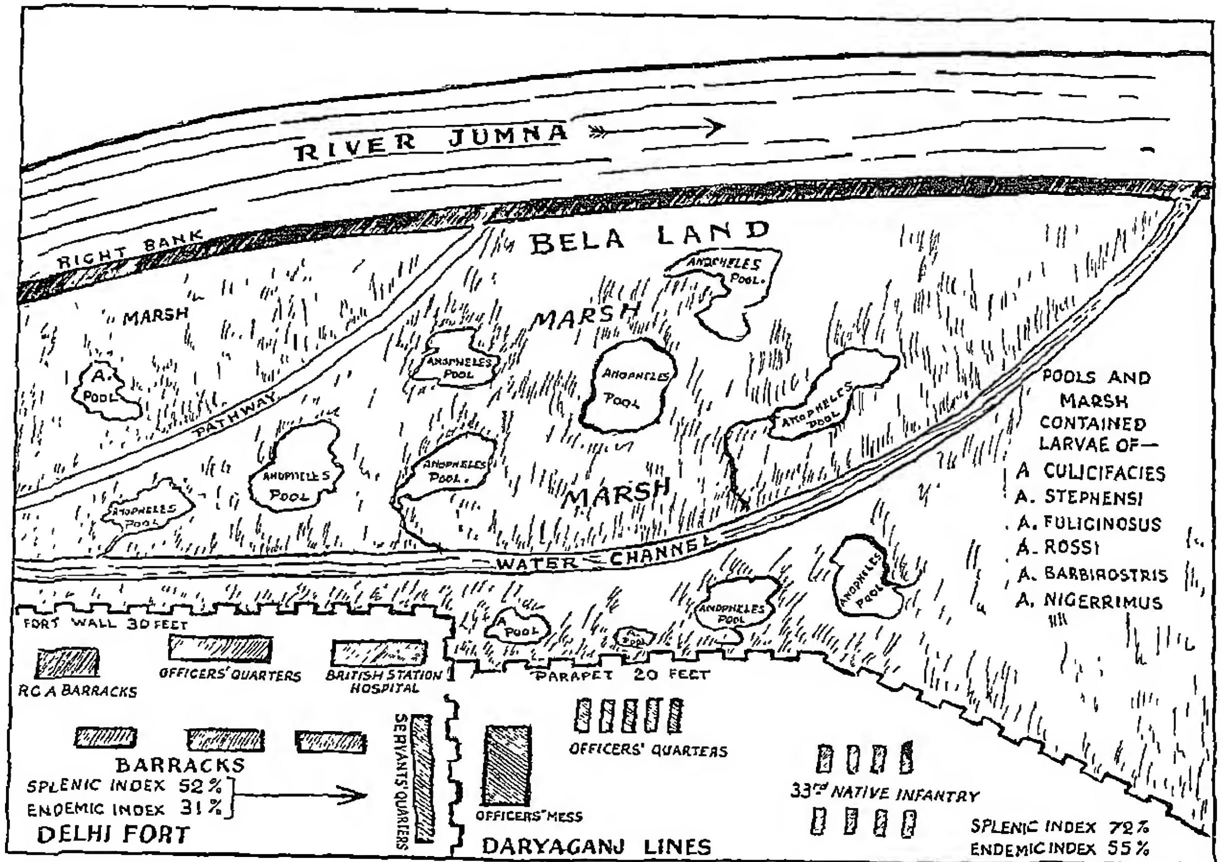


FIG. 45.—Rough sketch of Delhi (Old) Cantonment, showing part of Fort and the Daryaganj Lines (occupied by 33rd Native *Infantry*), and their relation to one another and to the *bela* land between the Fort and the River Jumna From memory and not to scale. September, 1909. The valid name of "*M rossii*" is *A. subpictus*, although the writer considers this an unnecessary and undesirable refinement in official nomenclature.

in India, but so far as the writer knows, search has not been made for the larvæ of mosquitoes in that country. They would, probably, be also contained in date and areca-nut palm trees. J. W. W. STEPHENS and S. R. CHRISTOPHERS visited a village in Madras with a fair amount of malaria. They searched everywhere for larvæ and only found one (*A. subpictus*), although there was plenty of water. There were, however, cocoanut palms. In Mesopotamia the writer never found mosquito larvæ in the irrigation moats around the date trees, but he remembers that one medical officer (Lt.-Col. J. F. DONEGAN, C.B., R.A.M.C.) at Kurna (a post on a low-lying triangular plot of land where the Euphrates joins the Tigris) expressed the conviction (March, 1915) that the Anopheles conveying the very prevalent malaria among the troops bred in the date palms which grew in thousands in and near the post. The local Arabs connected the date palms with malaria but not with mosquitoes.

Malaria considered as a local disease.—The whole cycle of malarial infection of man and Anopheles is in countless instances carried out within an area of 100 yards square or less. Every field worker knows this. The writer could cite dozens of instances in which the abolition of a simple small breeding place of mosquitoes has abrogated strictly local malaria. He will mention a few. In the early autumn of 1917, in Flashman's Hotel, Rawalpindi (Punjab), the guests were constantly getting attacks of benign tertian fever. In the Military Works go-down, 80 yards distant, were three discarded water carts containing swarms of *A. culicifacies* larvæ, and those of other mosquitoes, living in water replenished by the monsoon rains. The carts were removed; further infection in the hotel ceased. In September of 1909, when inquiring into the malaria of the Agra Cantonment, the writer found that all the occupants of the Government Telegraph Office and its outhouses were suffering from chronic malaria, some with benign, others with malignant, tertian fever. In the compound was a small circular pond of clear water 20 feet in diameter, fed by a land spring containing weeds, and partly shaded by a mango tree. In the pond were innumerable larvæ of *A. fuliginosus* and *A. culicifacies*. The water was at once kerosened, then pumped out, the excavation filled up with earth, and the spring diverted to the natural channel running outside the compound. The whole office and outhouses were fumigated with sulphur. By November this local malaria had ceased. In August of the same year at Bareilly the troops of two particular barracks in the British infantry lines suffered inordinately from benign tertian malaria. They shared one wash-house, the bath water for which was contained in two 400-gallon iron tanks, the iron circular covers of which were never applied. There were large numbers of *A. stephensi* larvæ breeding in the tanks. The substitution of a direct tap-water supply without storage abolished this essentially local malaria.

In September, 1909, the old Delhi Cantonment was one of the most malarious places in the Northern Command. The Fort and Indian Infantry Barracks (the old Daryaganj Lines), situated above the *bela* land (which is below the level of the Jumna), were infested with adult Anopheles (Fig. 45). The *bela* land was dotted over with pools, land springs, runnels of water and water-containing ditches in which the writer found the larvæ of *A. stephensi*, *A. fuliginosus*, *A. culicifacies*, *A. subpictus*, *A. barbirostris* and *A. nigerrimus*. In both the Fort and Daryaganj Lines large numbers of adults of the insects named (except the last two) were captured. The endemic index in Indian children in the Daryaganj Lines was 55, and the splenic index 72; the figures for those within the Fort being 31 and 52 respectively. The breeding-grounds were on an average 250 yards from the children's quarters. The problem here was an overwhelming one.

The following is a very interesting observation in connexion with a wider

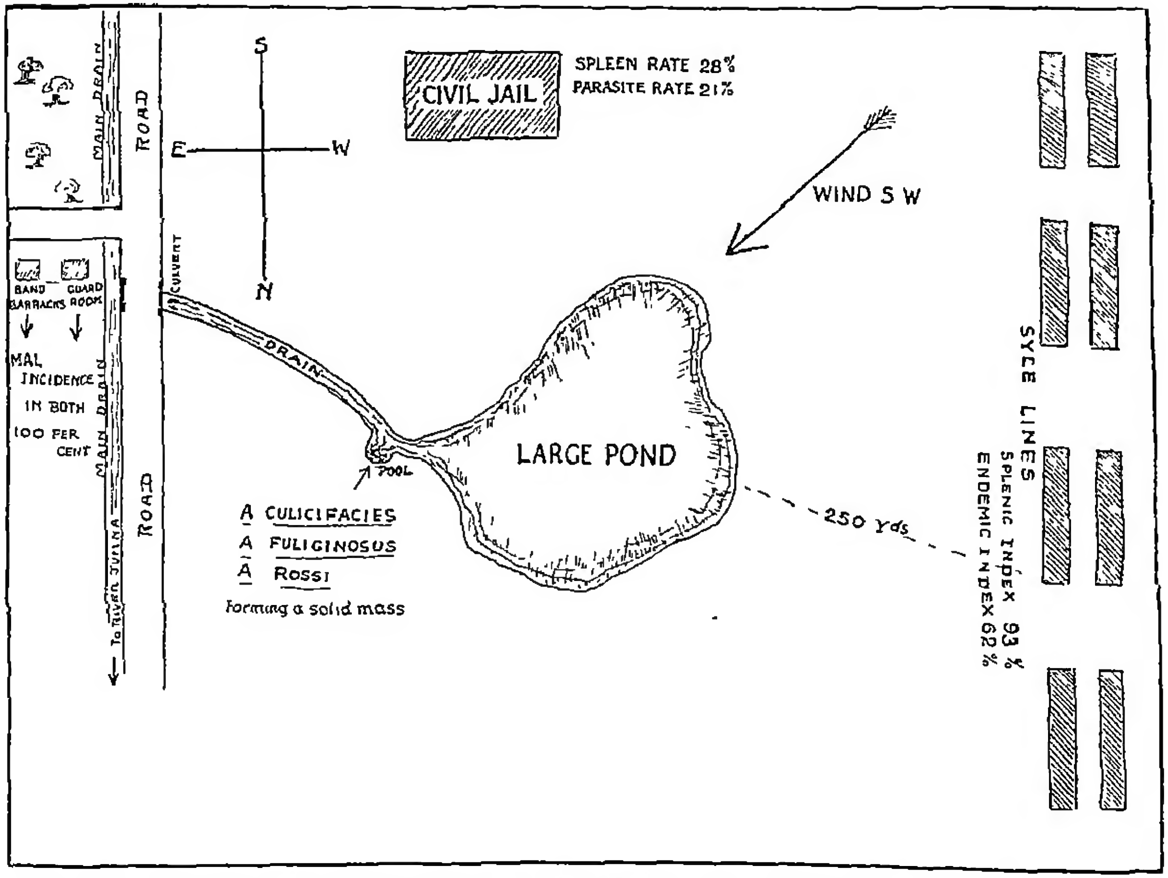


FIG. 46.—Plan of small area of south-west corner, Muttra Cantonment. Showing breeding-places of Anopheles. From memory and not to scale. August, 1909.

area of malaria from a common origin than those just mentioned. The writer was investigating malaria in the cantonment of Muttra in August, 1909; the barracks were occupied by the 15th Hussars. In the south-west angle of the cantonment were the syce lines, quarter guard, and band barracks, and to the west, the civil jail. A large pond was about equidistant from each of them. In the civil jail the spleen rate was 28 and the parasite rate 21; in the syce lines 93 and 62 respectively, while in the quarter guard block and band barracks the malarial incidence was 100 per cent.; the whole of the band was infected and practically every one who went on guard suffered. Malaria in the other barracks was slight. The pond referred to was the only breeding-place for anophelines discoverable in the neighbourhood. The writer searched the shores of this pond (which was irregularly oval in shape and about 90 yards long and 60 broad) without finding anything more than pupal cases of mosquitoes. At last he came to an outlet channel leading to a small bay; the overflow from the latter was carried by a *katcha* drain to the large station main drain that led to the Jumna (Fig. 46). The bay held about 20 inches of water, and the larvæ of *A. culicifacies*, *A. fuliginosus* and *A. subpictus* in it were so densely packed that they appeared like a solid mass from the surface to the bottom. It was a revelation to Lt.-Col. J G. HULBERT, I.M.S., who was civil surgeon, Capt. H E. KEANE, R.A.M.C., officiating O.C. Station Hospital, and to the writer. The larvæ were drifted to this one spot by the gentle south-west wind that had been blowing for days. A pint of kerosene oil destroyed the larvæ. The malaria in this part of the cantonment was subsequently easily controlled (Fig. 46).[1] The writer's experience in military cantonments has been that, with few exceptions, the maximum incidence of malaria occurs in barracks and quarters that are closest to the breeding-places of the local anopheline vectors of malaria.

Whilst anopheline larvæ are often absent from deep collections of water, such as large tanks with perpendicular banks, they are almost always to be found in large numbers in shallow tanks, large and small, especially in the shallower parts of these tanks, and their favourite breeding-places are the small shallow pools around these tanks of from 5 to 30 feet in diameter, when these are provided with grass and weeds. Corresponding favourite breeding-places are the small- and medium-sized pools in the beds of drying-up rivers. Taking them as a whole Anopheles prefer clean water containing weeds and cover.

Natural enemies of adult mosquitoes.—Adult mosquitoes are attacked by predacious insects of several kinds, such as spiders; by lizards; by insectivorous and night-flying birds, such as hawks; by flying bats. Ants are destructive to mosquitoes, especially when they are in small cages. It is advisable in any circumstance to stand each leg of the cage in a small tin containing kerosene oil or water. Nevertheless, mosquitoes multiply rapidly, and their numbers are so immense that their prevalence is only slightly restricted by natural enemies. Their surface is often covered by fungi, such as Entomophthora and Empusa, and by bacteria of various kinds. The ectoparasites of anophelines are usually hexapod larvæ of Acarines, which cannot be identified in the larval stage.[2] Parasitic water mites are often found on female Anopheles; whether they affect the mosquitoes injuriously is not known.

Enemies of larvæ.—There are many enemies of larvæ in natural waters, specially in large rivers, lakes and tanks, and these consist chiefly of fish, and larvæ of other larger insects. Constant disturbance of water is usually

[1] *Report of Malaria Survey of the 7th (Meerut) Division*—July-October, 1909, p. 82.
[2] STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed, p. 185.

and telluric conditions are favourable for so doing. We can get some notion of the vastness of the problem before us when we consider the astonishing rapidity with which mosquitoes multiply—eight mosquitoes can from the beginning to the end of the breeding season create a race equal in number to the entire human population of the globe.

(xvi) Study of Malaria Parasites in Infected Anopheles

First practise the examination of mosquitoes bred in the laboratory or by yourself. Get familiar with the normal appearances of the salivary glands (p. 76 and Fig. 18) and mid-gut (pp. 77, 78 and Fig. 19). Examine mosquitoes that have fed on healthy persons; follow this up by dissecting anophelines that have been infected by typical cases of human malaria. Carefully study sporozoites and zygotes in the dissections made. Much time and labour are saved by a few demonstrations of all this part of the work by an expert. Some will make more rapid progress by beginning on mosquitoes infected with avian malaria, especially Proteosoma in *Culex fatigans*; in any case, this latter interesting work should be undertaken at an early stage (pp. 115–117).

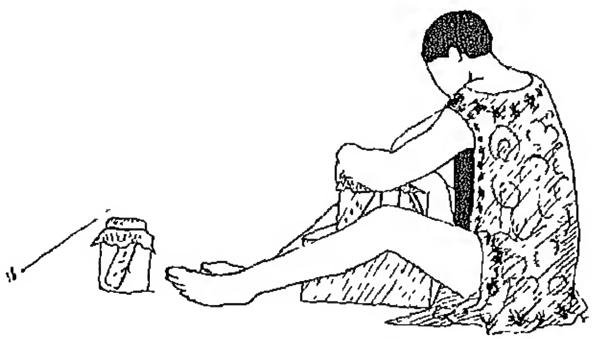


Fig. 47.—Method of feeding mosquitoes on human malarial blood

From Stephens and Christophers's *Practical Study of Malaria*, 3rd Ed.

To feed Anopheles on human malarial blood.—On the second evening after hatching or collecting in the way described on pp. 73–75, prepare bottles each containing twenty to thirty mosquitoes ready for feeding. Lift the bottle from the stopper, first disturbing any mosquitoes resting on the stopper, put it mouth downwards upon a small piece of mosquito netting (about 24 to the inch mesh) and tie this on with twine. "Shortly after dark take as many bottles as may be required to the ward or room containing the persons to be fed upon. Moisten the forearm of the patient, turn the bottle upwards, and let the forearm rest upon its mouth (Fig. 47). In working with anophelines, in from a few minutes to half an hour the bottle will be noticed to have splashes of blood upon the bottom and sides. It is well to wait until all the anophelines have fed, if this is practicable. Now take away the bottle, turn it upside down upon the table, untie the twine, remove the netting, and replace the bottle upon the prepared stopper. Repeat the process nightly, allowing the mosquitoes to feed by preference on the same case throughout. Every time the bottle is used add fresh water and a clean piece of paper."

Instead of the arrangement shown in Fig. 47, a mosquito-proof box like that shown in Fig. 41 for feeding mosquitoes on Proteosoma in birds may be used for infecting Anopheles with human malaria, the forearm being inserted through the sleeve on the left. Most mosquitoes will suck blood through netting, but some will not, though they feed readily in a larger space.

A light bird-cage covered with mosquito netting will answer the purpose; often in India one is obliged to be satisfied with a small, light packing-case covered on opposite sides with netting. A simple portable cage can be easily

unfavourable to their development; winds, which create surface waves, cause them to drift about or drive them to the bottom, and generally act detrimentally to them. In rivers, streams and canals we find them at the margins, attached to or under cover of leaves, grass, water plants, vegetable débris, etc. In canals the rate of flow is regular and less boisterous than that of rivers and streams, hence they are favourite breeding-grounds. In lakes we also find them near the edges. Lakes are generally stocked with many enemies of larvæ, and the mosquito, in laying eggs, selects the shallower parts, sides and margins. In ponds also larvæ live close to the edges. Many surface feeding small fish destroy them. A short account of the indigenous larva-eating fish of India is given in PART III, pp. 322–327.

In the natural state there is annually an enormous destruction of larvæ by the drying up of collections of water used as breeding-grounds by mosquitoes.

The following list includes the chief mosquito-larva consumers in water in India: Dragon-fly (AGRIONIDÆ) larva—the Demoiselle. It is very active and is found in great abundance in stagnant collections of water. It devours mosquito larvæ greedily. Larvæ of Mayflies (EPHEMERIDA), which are abundant and ubiquitous; larvæ of the aquatic families DYTISCIDÆ, GYRINIDÆ and HYDROPHILIDÆ, all of which are common and widely distributed; larvæ of some of the Chironomid midges; also certain predacious Culicid larvæ, such as *Chaoborus*, *Mochlonyx*, *Megarhinus* and others; water-bugs of the families NEPIDÆ or Water-Scorpions, NOTONECTIDÆ, CORIXIDÆ or Boatmen-bugs, and BELOSTOMATIDÆ or Giant Water-bugs. All these are found everywhere in ponds, ditches and sluggish streams. Larvæ of Caddis-flies (Trichoptera) are of ubiquitous occurrence in all natural fresh waters, and some of them are rapacious. Larvæ of Stone-flies (Plecoptera) in quick-flowing streams. Amphipod Crustaceans of the genus *Gammarus* are also mosquito-larva consumers. Miscellaneous foes include the fresh-water polyp Hydra, Dolichopodid flies and Anthomyid flies of the widely distributed genus *Lipsa*.[1] Bladderwort (Utricularia) entraps mosquito larvæ. Water containing the water-weed Chara (which is ubiquitous in India) is disliked by Anopheles for breeding. Duck and various water-fowl are credited with being devourers of mosquito larvæ.

Effects of heat on Anopheles larvæ.—Anopheles larvæ can only resist desiccation at 20° C. for two days, at 35° C. for one day, and at 40° C. for two minutes. Larvæ floated on to wet mud may live several days, but in India, when the mud loses its glistening surface, they perish.

We have much to learn regarding the habits of anophelines before we can effect their eradication from even limited endemic malarial districts. Observations in such districts will have to be carried out for some years before we can solve many of the unknown problems of to-day that harass the anti-malarial sanitarian. These inquiries may bring about improvements in our present methods of dealing with adult Anopheles and larvæ, or lead to entirely new methods of effecting their reduction. One of the directions in which profitable study and observation might be carried on is in the method of æstivation and hibernation of anophelines. It is during these periods of hiding that their numbers are comparatively few, and were we to know where to attack them in the larval and adult stages during the non-breeding seasons, we would certainly materially diminish the numbers appearing during the breeding season. In places where that season continues all the year round the task is very difficult. Destruction of hibernating mosquitoes is most useful because, if not carried out, the females, being fecundated, will deposit their ova as soon as the meteorological

[1] From Lt.-Col. A. ALCOCK's *Entomology for Medical Officers*, 2nd Ed., p. 70.

PLATE VIII

FIG. 1

FIG. 2

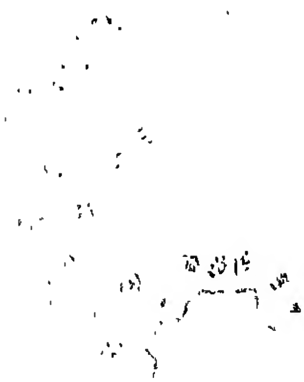


FIG. 3

FIG. 4

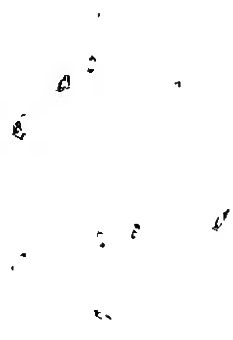


FIG. 5

FIG. 1. Young zygotes of the benign tertian parasite.
FIG. 2. Young zygotes of the malignant tertian parasite.
FIG. 3. Mature zygote, outside epithelium of mid-gut (section, hæmatein).
FIG. 4. Transverse section of salivary gland showing sporozoites *in situ* (hæmatein).
FIG. 5. Sporozoites from the salivary gland (Romanowsky stain).

(From STEPHENS and CHRISTOPHERS's *Practical Study of Malaria*, 3rd Ed.)

small proportion of the gametocytes sucked in by the anopheline undergo development in the tissues of the insect's stomach.

Different anopheline vectors fed on the same infected person develop different numbers of oocysts This may explain some of the failures of fed insects to infect man when there are but scanty oocysts.

Sometimes oocysts are found filled with black or brown bodies pervaded with pigment that is not malarial—the "black or brown spores" of some writers. Their nature is not definitely known, although some malariologists consider that they are degenerate oocysts that have not developed properly. These dark oocysts are liable to be infected with one or other of the parasites of the mosquito, *e.g. Nosema*, Microsporidia.

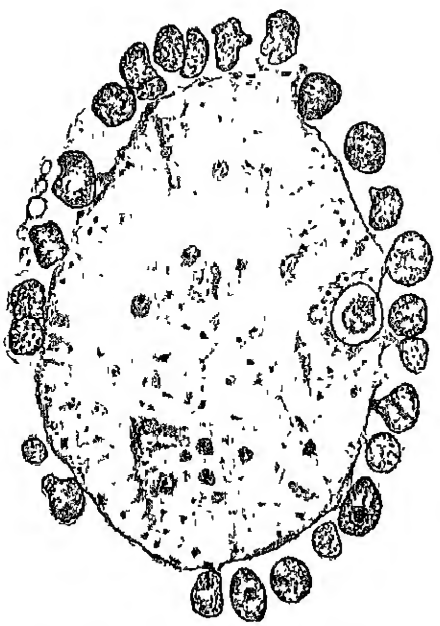


FIG 50.—Transverse microscopic section of stomach of *Anopheles maculipennis* with numerous oocysts in presporozoite stage (WENYON).

From MANSON'S *Tropical Diseases*, 8th Ed.

Examination of the sporozoite form of the malaria parasite.—Collect a number of Anopheles from native huts, from 2 to 10 per cent. or more will probably have sporozoites in the salivary glands in the malaria season. Otherwise use Anopheles fed and kept for twelve days or more at a temperature of 80° F. In neither case should *A. subpictus* be used. Dissect out salivary glands (p. 76). Press the acini with the point of a needle on the cover-glass; the secretion exudes into the surrounding fluid. Examine with $\frac{1}{6}$-inch lens. If sporozoites are present they are very numerous, and are seen everywhere in the fluid; the acini being also packed with them. Lastly examine with $\frac{1}{12}$-inch lens.

Sporozoites.—The sporozoite is a slender, slightly sickle-shaped body 14–15 μ long by 1–2 μ broad, sharply pointed at both ends with a thicker central portion in which the nucleus is lodged (Plate VIII, 5). Each moves rapidly by the contractility of its body, and has no flagellum. It possesses a single elongated or oval nucleus about its middle. Having reached the blood stream in man it speedily attaches itself by its anterior extremity to the surface of a red cell, which it gradually enters by its peristaltic contractions, associated with a vigorous to-and-fro movement of the whole body.[1]

So far as the writer knows, sporozoites of the different species are not distinguishable from one another.

Penetration of red cells by sporozoites.—This may be observed with sporozoites from a ruptured cyst in the stomach on a slide to which a little blood is added. After penetration the sporozoite, now called a *trophozoite*, contracts and becomes a small round or somewhat irregular "amœbula." A vacuole, large in proportion to the size of the parasite, is developed in the cytoplasm. The parasite grows at the expense of

[1] J D THOMSON and A. M WOODCOCK'S article, "The Parasites of Malaria," in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. II, p. 1517.

made, to fold flat, with bags of mosquito netting that can be drawn over the framework (Fig. 48).

To prepare fed mosquitoes for dissection.—After feeding the mosquitoes for a certain number of days, allow them to remain undisturbed, merely changing the water and paper each day. Note daily whether the anophelines have got rid of the blood from the mid-gut. When quite free from any dark coloration of the abdomen they are ready for dissection.

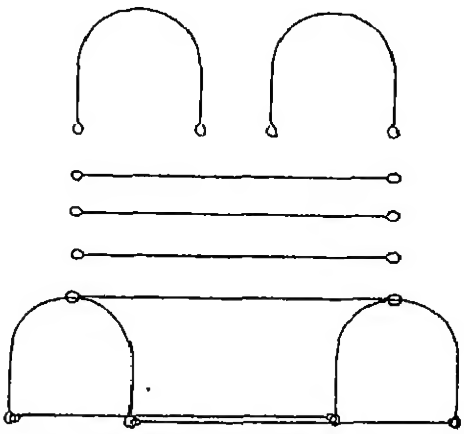


FIG. 48.—Represents straight and curved bits of stout wire to form the framework of a mosquito-proof cage.

From DANIELS and NEWHAM'S *Laboratory Studies in Tropical Medicine*, 5th Ed.

Examination of mid-gut for zygotes.—Collect a large number of anophelines from native huts, or use those you have infected. Keep them alive for two or three days until blood is no longer contained in mid-gut. Do not use *A. subpictus*. Prepare the mid-gut as stated on pp. 77, 78, on a slide with salt solution. Examine first with $\frac{2}{3}$- and $\frac{1}{6}$-inch lenses. Note the contents of the stomach, the respiratory tubes, muscle fibres, polygonal epithelium, and zygotes, if any. Look for clearly defined pigment in oval or round bodies. Many of the specimens will be negative; a small but variable percentage will probably be positive. Examine with a $\frac{1}{12}$-inch lens. In the positive specimens note the presence of small collections of malarial pigment. By careful focusing the younger forms of zygotes are seen as clear oval or round bodies 6 or 7 μ in diameter, in which the well-defined pigment occurs. The more advanced forms are very obvious. Zygotes of malignant tertian malaria, when young, show a clump of pigment resembling black pepper; those of benign tertian show yellowish or golden pigment in wisps or strands; those of quartan show rather coarse pigment in a clump.

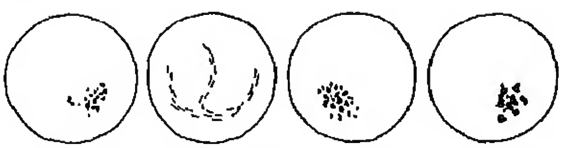


FIG. 49.—(Left to right.) Zygotes of malignant tertian, simple tertian and quartan malaria and Proteosoma.

From STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed.

A sporoblast may show radiation. A large cyst may show many fine sickle-shaped bodies—the sporozoites.

Older zygotes (40–60 μ) may show a well-defined oocyst wall, the formation of sporoblasts; in a more advanced stage the sporoblasts are seen to be surrounded by a radiating arrangement of young sporozoites or blasts. Fully developed forms are large cysts packed with many hundreds of fine sickle-shaped bodies, and if they are ruptured, these latter escape into the surrounding fluid and are distinguished with a $\frac{1}{8}$-inch lens as sporozoites (Plate VIII, Figs. 1 to 5).

From laboratory studies it has been repeatedly demonstrated that only a

squares, micromillimetre scale and camera lucida. Thoma-Zeiss hæmocytometer, Tallquist hæmoglobinometer,[1] Cornet's forceps, straight surgical needles; slides, cover-slips $\frac{7}{8}$-inch diameter, glass rods, stoppered jars 13 × 7½ centimetres; porcelain dishes, square, flat, 4 × 4 inches, for fixing and staining; drop bottle for xylol; watch-glasses; Petri dishes; copper dish for boiling slides; spirit Bunsen; methyl alcohol (pure, obtained in tubes); absolute alcohol; cedar-wood oil; xylol; Canada balsam; distilled water; drop bottle, pipette. Leishman's stain—in "Soloids" (Burroughs, Wellcome & Co.), 0·015 gramme each, or in powder. Giemsa stain is useful for certain special observations; some prefer it for general use in malaria work; best obtained ready made.

The microscope.—A heavy, substantial broad-based stand is desirable. The objectives should give a sharp and clear definition and the field should be flat. Achromatic objectives give a flatter field than the apochromatic ones. A good oil-immersion lens, preferably a $\frac{1}{12}$-inch one, is indispensable. It is, of course, possible with a good system of dry lenses reaching 500 diameters to recognise malaria parasites, but it is a strain, especially with fresh-blood preparations. It is frequently necessary to know with some degree of accuracy the actual powers we are working with. The following table[2] gives, approximately, the magnification with English and Continental combinations of eyepieces and objectives:

English (Watson's).			Continental (Leitz's).		
Eyepiece	Objective	Magnification	Eyepiece	Objective.	Magnification.
2	$\frac{2}{3}$ inch	80	2	3	62
4	"	132	4	3	103
2	$\frac{1}{6}$ inch	203	2	6	288
4	"	488	4	6	480
2	$\frac{1}{12}$-inch oil immersion	672	2	$\frac{1}{12}$-inch oil immersion	630
4	$\frac{1}{12}$-inch oil immersion	1,120	4	$\frac{1}{12}$-inch oil immersion	1,050
Tube length, 160 mm.			Tube length, 170 mm.		

The objective lenses require the greatest care. They should be kept free from dust and mould, and be always thoroughly cleaned before being put away. If a bell jar is used to cover the microscope left on the working-table it should rest on a piece of chamois leather or similar material. In practice the microscope and lenses are not put away. Perhaps wrapping up the whole microscope with its attached lenses in a duster criss-cross is most convenient. From time to time examine the inside of the objectives, as dust gets on to the back of the lens down the tube. Lenses are cleaned after use with a soft rag or silk dipped in xylol or alcohol.

Camera lucida, etc.—A camera lucida is a most useful acquisition, especially for those who are not good draughtsmen. Leitz's is one of the easiest to use. A *micrometer* slide ruled to $\frac{1}{100}$ of a millimetre is almost indispensable. It should be used to

[1] This is, of course, only a very rough-and-ready means of estimating hæmoglobin and should not be used in scientific investigations. Probably the most reliable hæmoglobinometers are Haldane-Gowers', in which the standard is said to be permanent, and Fleisch's, in which it is of glass

[2] From DANIELS and NEWHAM'S *Laboratory Studies in Tropical Medicine*, 5th Ed.

the hæmoglobin, as indicated by the appearance within it of pigment granules. It assumes a ring form which is usually thicker at one part than the rest.

Movements of sporozoites.—Dissect out the salivary glands and transfer to a drop of human serum previously obtained by allowing blood to clot in a small tube. The sporozoites will be seen to move by forming curves, by ring-formed contraction and forward motion.

Permanent preparations of sporozoites.—Press the cover-glass firmly on the salivary glands and glide it along the slide; a film is formed on both the slide and cover-glass, on one of which the salivary glands lie. Dry rapidly in air. Wash, dry, stain with Leishman and examine (without cover-glass) with a $\frac{1}{12}$-inch oil immersion lens.

To determine the percentage of Anopheles infected with malaria parasites—the sporozoite rate.—Collect a large number of anophelines from the houses, huts, etc., of the neighbourhood in which malaria is being investigated. Dissect (pp. 76, 77) as many of these insects as possible, noting in each case the species, and in which species, if any, sporozoites are found. Frequently it will be discovered that the sporozoite rate is very small, notwithstanding that the anophelines are in abundance and the endemic index moderate. It varies greatly in different endemic areas. The writer has found it to be from 0·6 to 13 per cent. in the malaria season. Keep for several days specimens not dissected and then examine the mid-gut for zygotes. Hereditary infection of Anopheles does not occur. (See Appendix VI—3, ii.)

K.—THE MALARIA PARASITES OF MAN IN INDIA

In the present section there are considered: the microscopical examination of normal blood, fresh and stained; accidental fallacies in blood films and fallacies arising from bodies simulating parasites in fresh and stained specimens; malaria parasites and their classification; their three forms, the question of their specific unity or plurality; their position, whether intra-corpuscular or extra-corpuscular. Lastly, there is given a brief account of the artificial cultivation of malaria parasites.

(I).—Microscopical Examination of Normal Blood

Before commencing the study of malaria parasites it is well to become thoroughly familiar with the microscopical characters and appearances of normal blood in both fresh and stained specimens, the different varieties of leucocytes, the size, colour, shape and appearances of red cells, etc., the appearance of artefacts, vacuoles, fissures, variations in crenation and buckling in red cells, ordinary dirt, and hæmaconia or blood dust, to recognise deposits of stains on the red cells, and the various forms assumed by the squashed nuclei of leucocytes, the different forms and appearances of platelets in stained films whether in clumps or singly, and to be able, without any hesitation or doubt, to tell whether a stained blood platelet on or under a red cell is a malaria parasite or not.

For a complete account of the microscopical characters of normal human blood the reader is referred to works on hæmatology.

Apparatus required for blood examination in malaria.—Microscope (with large stand), complete with Nos. 2 and 4 eyepieces, 3 objectives—$\frac{2}{3}$-inch, $\frac{1}{6}$-inch and $\frac{1}{12}$-inch oil immersion lenses, sub-stage condenser, iris diaphragm, mechanical stage, stage micrometer, micrometer eyepiece with scale or with

A drop of blood[1] is received on the centre of the slide and the cover-glass gently lowered on to it. Or, touch the apex of the droplet with the cover-glass held by the rim between the forefinger and thumb, and drop the cover-glass on to the slide (Fig. 51). If the blood is not to be examined at once it should be ringed with vaseline, when it will keep for some hours. In a well-made film three zones are seen. The edge of the film (Fig. 51, *a*) is thick and irregular; here the red cells are in rolls or masses; it is too thick for examination of the individual corpuscles. Internally to this is a ring with a slightly opaque or ground-glass appearance. Here the red cells are lying flat and not to any great extent overlying each other (*c*). The centre of the film is clear and transparent and the corpuscles are scanty (*b*); this part of the film is composed almost entirely of plasma. In fresh-blood films it is very desirable that the blood corpuscles should be separate from each other and in a flat layer.

To get good fresh preparations it is imperative that both slide and cover-slip be free from grease; if they are not, spreading is interfered with; grit must be absent, this being assured by rubbing the slide and cover-slip thoroughly with a soft clean rag immediately before use. The droplet of blood should be so small that it does not extend to the circumference of the cover-slip; if the droplet is too large the cover-slip floats in the plasma and there is room for many *rouleaux* of red cells to be formed.

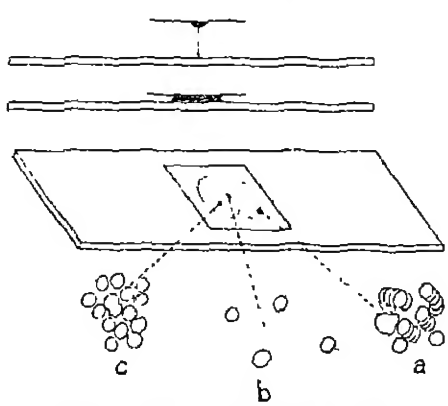


FIG. 51.—Making a fresh-blood film.

From DANIELS and NEWHAM's *Laboratory Studies in Tropical Diseases*, 5th Ed.

Microscopical examination of fresh- and stained-blood preparations.—In fresh preparations the light must be shut off to such an extent that the field is first clearly seen; too little is better than too much light, as the early stage of the parasites of malaria is difficult to see in a bright light. Fresh blood shows the red cells, different forms of leucocytes, blood platelets, hæmaconia or particles of blood dust, which appear as refractive granules with brownian movement; after some minutes fibrin in the form of a delicate network will be observed to develop in the film. With fresh malarial blood the beginner should first look for red cells containing pigment granules. These will be found in the intermediate or older stage of development of the asexual parasite. Later he should look for the smaller, opaque unpigmented or slightly pigmented forms.

To make blood films.—In adults and children the palmar aspect of the pulp or tip of a finger is to be pricked. Some prefer the back of the finger

[1] Does the first droplet of blood or the second give us an average specimen as regards the number of erythrocytes infected and non-infected, and does it matter in this respect whether the droplet is taken from the finger tip or the lobe of the ear? Prof. J. W. W. STEPHENS is about to publish the result of observations which show that the first drop of blood from the ear always contains more parasites. We know from LUCEY's work (*Trop. Dis. Bull.*, 1922, p. 290) that as regards large mononuclears the first drop of blood from the lobe of the ear may contain 35 to 41 per cent. of large mononuclears, the normal being 7 per cent., Prof. J. W. W. STEPHENS made the same discovery as regards ear and blood, and states that "in some ears the first drop looks like leukæmic blood."

standardise a focused eyepiece micrometer or to draw a permanent scale, by the camera lucida, upon a piece of Bristol board on the table. Measurement of any object can then be effected by the micrometer scale or by the camera lucida.

Slides and cover-slips.—The thin white slides do not give the same wear as those of coarser quality; No. 3 is the best to use. They require thorough cleaning, and a stock, cleaned and ready for use, needing only wiping, should be at hand. The best and thinnest quality of cover-slips (No. 1) are required for blood work; some of the thicker kind are necessary for coarse work; they stand rough usage. The original stock of cover-slips should be packed in oil.

In connexion with the Thoma-Zeiss *hæmocytometer* it is essential that the pipettes should be thoroughly cleaned each time after use; if this is not done they will be rendered useless. Blow out the contents and fill the pipettes a few times with water, suck in acid-alcohol (1 per cent. HCl), get rid of it, and subsequently dehydrate with equal parts of alcohol and ether[1]; dry the pipettes thoroughly in an incubator or put in a dry, clean, warm place.

Those who are engaged in hæmatological work usually carry with them a small case containing straight surgical needles, slides, and a few glass curved tubes or capsules for blood for making sera diagnoses. Such a case can be made out of a piece of chamois leather, folded like an ordinary pocket letter case, and containing a few pockets for the slides, etc.

Necessity of cleanliness in blood examinations.—*Cleanliness is of great importance*; it gives reliable results and considerably lessens the chances of erroneous conclusions being drawn in doubtful cases.

To clean dirty slides.—Blood-film slides no longer required for the moment should be put aside to be cleaned; never throw them away, as they will often be wanted. Rub with turpentine, benzene or xylol to remove any adherent oil or grease. Wash with soap and water, rinse in clean water, dry and rub thoroughly with a clean cloth. Or, boil the slides for a few minutes in a strong solution of ordinary washing soda. Then wash in tap water. Place in 25 per cent. of sulphuric acid for five minutes and then wash in running water; let all the water drain from the slides and place in a well-corked wide-mouthed bottle containing methylated spirit. Rub the slide thoroughly with a clean soft rag before use. For ordinary work it is usually sufficient to dip the slide in water and *wipe dry* with a clean soft cloth. Some of the "Monkey Brand" soaps with a few drops of water will get rid of grease.

To clean cover-glasses.—Boil in a porcelain dish for ten minutes with bichromate solution.[2] Wash in water till all yellow colour has vanished. Drain off water and keep in methylated spirit in a wide-mouthed, well-stoppered bottle. In heating the bichromate solution use a small flame; otherwise it splutters and stains everything it falls on. When required remove a cover-slip with a forceps, dry with a soft clean rag. Cover-slips must be free from grease, mould and grit.

To clean the skin.—In ordinary circumstances all that is necessary in malaria blood work is to wipe the skin with a clean dry cloth. In Indian bazaars and villages this, as a rule, is all that can be done. If special cleanliness is called for, wipe with cotton-wool or a clean rag soaked in ether, dry, then repeat with alcohol.

Fresh preparations.—The needle should not be too fine. Sterilise it in a flame before use. Keep it in absolute alcohol or in a well-stoppered glass tube. Use a perfectly clean and dry slide and cover-glass. Prick the finger.

[1] Only the purest ether should be used; impure ether leaves a deposit.

[2] Bichromate of potash 2 parts, sulphuric acid 3 parts, water 25 parts.

surfaces, slide them apart. Dry in air, stain in the same way as ordinary slide films, and lower on to the centre of a slide holding a drop of Canada balsam.

Fixing films.—No fixative is required with Leishman's liquid stain. For ordinary Romanowsky the best fixative is *absolute alcohol*; the alcohol may be kept in a wide-mouthed glass-stoppered bottle, and the films placed in it for about five minutes. For Giemsa pure methyl alcohol, absolute alcohol, or equal parts of absolute alcohol and ether may be used. *Heat should not be used for fixing blood films* except in some special methods of staining, such as Ehrlich's tri-acid stain, in which heating is an essential part of the process. It is necessary to remember that before the film is fixed the hæmoglobin of the red cells is dissolved by water if it comes into contact with them. The smallest amount of moisture is detrimental to staining. So much so is this the case that the moisture of the air during the monsoons, the mere breathing on the slide, or atmospheric moisture absorbed by the alcohol used for fixing, are all sufficient to give defective results.

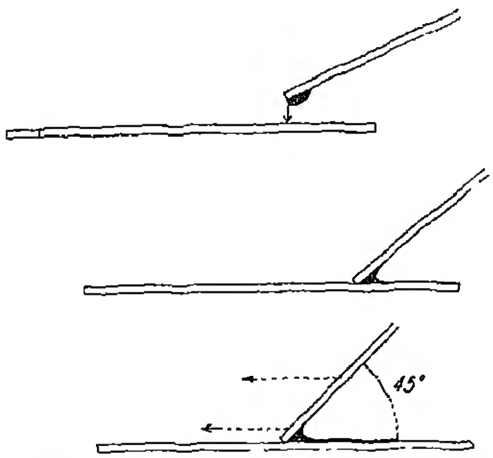


FIG. 53.—Method of making dry blood film with two slides.

From DANIELS and NEWHAM'S *Laboratory Studies in Tropical Diseases*, 5th Ed.

Romanowsky stain.—In studying malarial Plasmodia, the original Romanowsky stain mentioned above, or one of its modifications (Leishman, Giemsa, Jenner, Wright, Ziemann), is essential; any one of these stains the chromatin of the nuclei of parasites red, and the protoplasm blue. The basis of all Romanowsky stains is as follows "A solution of methylene-blue that has been acted upon by carbonate of soda or other alkaline reagent, becomes partly converted into various polychrome derivatives, *e.g.* methylene-azure and methylene-violet. These bodies are in solution. When they are acted upon by a solution of eosin there results a precipitate, and this precipitated body (or bodies) possesses the property of staining the nucleus an intense heliotrope-red colour (chromatin stain)."[1] The precipitate has a special affinity for chromatin The staining may be effected at the moment of original precipitation; or the precipitate may be re-dissolved in a solvent such as methyl alcohol (as occurs in Leishman and Giemsa stains), and finally be precipitated out of solution by the addition of water at the time of staining. The various modifications of Romanowsky stain give satisfactory results for quick work. Purity of the stain is indispensable. Particular attention must be given to each stage of the staining process. Leishman's stain, whether in tabloids or crystals, is convenient to carry about; both it and pure methyl alcohol are now procurable at all large chemists in India. Films so stained soon fade in India if mounted in Canada balsam (see below).

Leishman's stain.—This is the precipitate from the action of a watery solution of eosin on a watery solution of methylene-blue *previously treated*

[1] STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed., p. 21.

just above the root of the nail. In young infants the lobule of the ear is more convenient. In using the finger wrap a piece of bandage or tape tightly round it in a spiral. The prick with the needle should be made pretty firmly and sharply, but not deeply. One of the operator's fingers may, if necessary, be kept against the needle about $\frac{1}{10}$ inch from the point; this safeguards from too deep penetration.

The droplets, which should not be larger than the head of a pin, are received on the slides about $\frac{1}{2}$ inch or so from the end. The middle of the shaft of the needle is laid on a droplet and allowed to remain for a second until the blood has spread along the shaft between it and the slide. The needle, held by the pointed end, is now carried smoothly along the slide to the other end (Fig. 52); it should be held just close enough to the slide to take up the droplet. The spreading edge is then less broad than the slide. To make films with even, straight edges, it is a good plan to keep the end of the thumb in contact with the edge of the slide as the needle glides along the latter. Dry by waving the slide to and fro in the air.

A slide may also be used as a spreader, one corner or both corners of one end being snipped off or rounded with a file. It should be of the best quality with ground edges. A good film should have at least one clear edge. The droplet of blood is received about $\frac{1}{2}$ inch from one end of the film slide. Lay the spreader in contact with the droplet and allow the latter to run along between the spreader and the film slide; hold the slide-spreader at an angle of, say, 30°, then move the spreader gently and evenly along the whole length of the slide. Do not use any pressure or many of the red cells will be damaged. A thin, even and uniform film is obtained. The slide is then moved through the air rapidly until the film is dry. The more rapidly the blood dries the better the red cells remain for staining. The film should be thin and uniformly spread—a single layer of red cells just barely or not quite touching each other is the object aimed at. As far as possible the upper and lower edges of the film should have a straight line parallel with the edges of the slide; this helps in making a differential count of the leucocytes, should that be necessary.

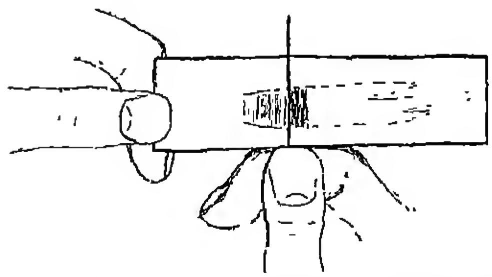


FIG. 52.—Author's method of making thin blood films.

Daniels's method.—This is a modification of the foregoing. Place a small drop of blood half an inch from one end of an absolutely clean, dry slide. Apply one end of another slide to the drop and, as soon as the blood has run along it, move the spreading slide at an angle of 45° to the other end of the blood slide held horizontally. The blood is drawn or pulled behind the edge of the advancing slide and not pushed along. An angle of less than 45° makes a thin film, a larger angle a thicker one. The film is even and made of any desired thickness, and crushing of red cells is eliminated. Beautiful preparations may be obtained by this method. It is advisable to round off the angles of the slide used as a spreader.

Cover-slip blood preparations.—Cover-slip preparations are made by placing a small drop of blood on the centre of a clean cover-slip and letting it fall gently on another slip, and when the blood has spread over the two facing

diluted by adding one drop of it to 17 minims of water and shaking thoroughly. Do not be tempted to add more than one drop to the 17 minims, otherwise the staining is impaired. The films, blood side downwards, and resting by the ends on glass rods, are placed in a Petri dish and the stain poured into the latter. Allow the stain to act for fifteen to thirty minutes; the film is then flushed with distilled water, and dried with filter paper.[1] The strong Giemsa solution may be purchased from the better-class chemists and from the Kasauli and Parel Laboratories.

Get thoroughly familiar with one of the Romanowsky stains and all its peculiarities in staining normal and malarial blood under varying circumstances and adhere to it Leishman will be found very satisfactory; Giemsa runs it closely. With stained preparations, after preparing and drying the film, a drop of cedar oil is dropped on to the stained blood and the oil immersion brought down to it. It is unnecessary to use Canada balsam and a cover-slip. If the slide is required for further examination at a later date, allow a few drops of xylol to fall on the cedar oil, drain it off and dry; the xylol removes the cedar oil; then put the labelled slide away in the cabinet.

When a preparation is ready for examination the condenser is racked up, the immersion lens lowered with the coarse adjustment and finally focused with the fine adjustment focus upwards first, then, if necessary, downwards. If this is done there is no risk of jamming the objective lens through the slide. Begin examining at one edge of the film and then go towards the forked or tongued part; it is along the edges and the forked part that parasites are usually more numerous when present.

Blood films that have to be despatched any distance by post or otherwise for examination should be fixed before despatch to prevent mould developing on the surface; this is particularly necessary during the monsoons, when the air is hot and moist.

Thick blood film.—The thick blood film is useful for detecting malaria parasites when they are scanty; it is specially valuable for finding crescents and trophozoites old enough to contain some hæmozoin; less satisfactory for the first stage of the ring forms. It is also a good method of finding "carriers" in healthy people; also when it is urgently necessary to make a diagnosis in a doubtful case, e.g. latent malaria in an operation case. It requires an expert to be quite sure of a single "ring" in a thick film. A moderately large drop of blood is received on to a slide and spread gently over the area of a sixpence; it is thoroughly dried in the incubator or cautiously over a flame in all seasons but the summer; then the hæmoglobin is removed with acid-alcohol (glacial acetic acid 1, alcohol 8) or acid-formalin and stained in the usual way. Dry thoroughly before staining with Leishman's stain. If Giemsa's stain be employed the films should be stained while wet. Remember that acetic acid (which is volatile) on a slide may entirely upset the staining of neighbouring films. The fixing is very important, especially if the slide will not be stained for a few days.

Ross's thick film.—Allow five or six drops of blood to fall on the centre of a slide so as to cover an area 6–8 mm. in diameter, and spread so that the film forms a uniform layer. *Dehæmoglobinise in water*, dry in air, and stain with Leishman or Giemsa stain.[2] The parasites will often be found somewhat deformed by the action of the water in dehæmoglobinising the film. All thick-film methods require some experience in their use if errors are to be avoided.

[1] BYAM and ARCHIBALD's *Practice of Medicine in the Tropics*, Vol. I, p. 530.
[2] MANSON's *Tropical Diseases*, 8th Ed., p. 823.

with an alkali, such as carbonate of soda. The precipitate is washed and dissolved in methyl alcohol. In making the stain we employ methyl alcohol and Leishman's stain in "soloids" or powder. Three "soloids" (Burroughs, Wellcome & Co.) are powdered in a glass mortar and the methyl alcohol added by degrees. In using the powder 5 grains are placed in a watch-glass, then a drachm of methyl alcohol is added; stir with a glass rod. Allow to settle and pour off into a drop bottle. Add more alcohol and stir again; then pour off, and so on until all the powder is taken up. The stock solution of this does not keep well in India.

Staining is effected thus: "The film is made and dried in air. Pour on 15–20 drops of freshly prepared unfiltered stain; leave for thirty seconds and allow the methyl alcohol to fix the film. Add double the quantity of distilled water. Mix by gently rocking the slide. If the stain is good a scum forms at once. Stain for five to ten minutes. Let the films during this time rest on glass rods in a Petri dish, covering all with a bell-jar to prevent evaporation and the formation of granular deposit. Float the stain and the scum off by pouring distilled water on to one end of the slide. Do not pour the stain off or the scum and débris will be left behind deposited on the film. Soak the film in distilled water for thirty seconds, or until the red corpuscles are pink; dry with filter paper, or by placing it slanting against a stand. If there is a deposit on the film wash *rapidly* in 60 per cent. alcohol followed by distilled water, dry quickly and mount."[1]

In the writer's hands this has been found the most satisfactory of all the Romanowsky stains for malaria parasites, and the most uniform in its results. The red cells have an orange to pink colour; nuclei have shades of violet; eosinophile granules are red; neutrophiles are yellow to lilac; blood platelets, purplish, malaria parasites blue, the chromatin being metallic red to rose pink. In the Romanowsky stains mentioned it is advisable to use distilled water, which should be kept in stoppered bottles. After use the stopper should be replaced at once to prevent organisms from the air gaining access.

Leishman-stained films tend to fade; if the preparations are to be kept for some time a little overstaining is desirable. This may be secured by initially covering the film fully with the stain for *one minute*, rocking as before, then adding about an equal quantity of distilled water and allowing it to remain for ten minutes or so. Now flush off with distilled water until the film has a light mauve colour—ten seconds are usually required—then dry carefully with filter paper. Should a precipitate appear on the film it is readily removed by pouring a few drops of undiluted Leishman stain over the film and then flushing with distilled water.[2]

The best staining results are obtained with fresh unfixed films. In old and fixed films the hæmoglobin takes on a bluish tinge instead of the clear pink of the freshly drawn blood. In using Leishman's stain with old films DANIELS and NEWHAM advise staining in the usual way up to the stage of the clearing process, and then, instead of using distilled water for that purpose, flood the slide with a 1 per cent. solution of acid sodium phosphate. In a short time a great deal of the blue colour will be removed and the usual pink become visible. When it is pink enough, flush the slide with distilled water and dry. A 10 per cent. alcohol (which the writer always employs) will do the same, but not so well.

Giemsa's stain.—This is made up of azur II–eosin 3 parts, azur II 0·8 part, glycerine (pure, Merck) 250 parts, methyl alcohol 250 parts. In using it, fix the films in *absolute* alcohol or pure methyl alcohol, or in equal parts of absolute alcohol and ether, for ten minutes; allow them to dry. The stain is

[1] BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. I, p 529.

[2] R. G ARCHIBALD in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. I, p. 530.

slides. They have a well-marked abrupt edge; are free from granules and are never opaque. They never show amœboid movement, nor the differentiation of a parasite into its component parts. Focusing up and down and changing the illumination of the field as a rule enables their nature to be recognised. They do not contain pigment. Central vacuolation in red cells is not uncommon in malarial anæmia and may be mistaken for a non-pigmented young parasite. But malarial rings are usually at or near the periphery of the red cell and do not vary in size when we focus up and down. Stained vacuoles may also mislead. This artefact, when met with, will be seen in many of the cells of one or more areas and absent in others; they are devoid of the red, white and blue of stained parasites. Vacuoles are real pitfalls for beginners, both in fresh and stained preparations.

Misshapen erythrocytes presenting a granular area, which is sometimes roughly crescentic in shape (Fig. 55, 2, *a*), may be misleading; here the entire absence of pigment should prevent error being made.

Blood platelets (hæmatoblasts).—These are colourless refractile bodies from 1 to 3 mm. in diameter. They are a frequent source of error. The mistake is most common in stained preparations when a single platelet lies on a red cell. It has not the distinct outline of a parasite, and it is surrounded by a clear unstained border arising from the hæmoglobin of the red cell having been displaced. "The platelet, devoid of protoplasm, is without any blue-stained part; its chromatin is granular, irregular and without any definite shape; it has not the ground-glass character of a parasite. The platelet as a whole shows nothing like the divisions of a parasite into red nucleus, blue cytoplasm, unstained vacuole; it has no pigment. When grouped together they may give the appearance of a sporulating parasite, but their granular and irregular chromatin, embedded in cytoplasm which has a somewhat reticular structure with an indefinite outline, together with the absence of pigment, will help to differentiate them."[1] "Red, white and blue" are the safest criteria for the tyro in distinguishing rings. It is quite easy to mistake a leucocyte for a full-grown parasite, and *vice versa*. Free platelets may also be mistaken for crescents; the absence of pigment should distinguish them. Occasionally both in films and spleen smears they may show a faint resemblance to *Leishmania donovani*, but they are devoid of the definite nucleus and striking kineto-nucleus of that body. Malaria parasites are identified from platelets, stained vacuoles, leucocytes and deformed red cells by carefully examining the red blood cells in stained specimens for small bodies showing—the *red* dot of the chromatin nucleus, the *blue* protoplasm of the parasite, and a *white* vacuole in the blue.

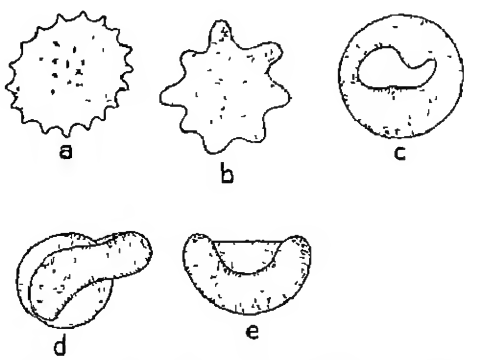


FIG. 54.—*a*, *b*, Crenated corpuscles; *c*, vacuolated corpuscle; *d*, *e*, buckled corpuscles.

From DANIELS and NEWHAM'S *Laboratory Studies in Tropical Diseases*, 5th Ed.

Fissures or cracks in erythrocytes (Fig. 55, 0, *f*), on focusing, show refrac-

[1] R. G. ARCHIBALD in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol I, p. 540

M. A. BARBER and W. H. W. KOMP's [1] *thick-film method*.—The following thick-film method removes the factor of loss of time in making these films. A thick and a thin film are made on the same slide. The slides are numbered *in* the thin film and the numbers recorded in a notebook They are placed in a slide box on end and the box closed. Pieces of cardboard (about 1 inch × $\frac{1}{16}$ inch) are dropped between the thin smears of the slides, one to each interval. All the slides in one box (say 25) are kept together in a block by means of a stout rubber band and given one label. The thick-film end of the block is now stood in water without wetting the cardboard or thin film. No alcohol or acid is used for dehæmoglobinisation or decoloration. After dehæmoglobinisation the block is carefully rinsed and then, without drying, stained for about $\frac{3}{4}$ hour. The stain is put into any vessel of such a size that the stain is of sufficient depth to cover the thick films without wetting the thin films. Move the block in the stain occasionally to ensure uniformity of distribution. If overstained place for a few minutes in water; dry the block by placing it on its edge. The rubber band is not removed until the slides are to be examined microscopically. The devisers of this method strongly advise the Giemsa stain. They add 75 c.c of water to 1·25 c.c. of the stock stain for twenty-five slides. It has recently been shown that Leishman's stain also gives excellent results.[2] It seems to be important to use water with a proper pH, such as fresh rain-water. About $\frac{1}{8}$ c.c of blood is recommended for each film, although less may answer The thin film is not stained unless the thick film fails to give the required information. An intelligent assistant can be taught this method in a short time. BARKER and KOMP have used it for many years in making malaria surveys, and have found it both helpful, reliable and time-saving. They claim that it brings out adult schizonts and gametocytes most distinctly when they are very scarce. It assists in diagnosing the type of malaria when, say, only a few young trophozoites are present on the thin film, as the thick film will probably have a few older or developed forms the spores of which can be diagnosed

The writer has no experience of this method. He sees in it a rapid way of dealing with a large number of films in the worker's laboratory, the clinical laboratory of a hospital, or in clean surroundings, but it must still be considered rather a coarse method of procedure. *From his very unsatisfactory results with thick films in malaria surveys in India he is unable to recommend this or any other thick-film method in the field*; the drying process takes too long, and by the time the film is dry it has become surcharged with animal and vegetable organisms from the dust-laden air, to say nothing of what it gathered from the children's dirty fingers. The only condition in which it could be used in field work is when moving about with a mobile laboratory (motor) so that films can be at once transferred to the incubator to dry. The thick film is a useful accessory, but should not be used as a substitute for the ordinary methods of blood examination in malaria

Accidental fallacies in blood films.—These will have been previously studied in histological laboratories. The more common are hairs of man and animals, cells and hairs of insects. The ordinary water, or even distilled water, used in staining may contain protozoal or infusorial forms, spores of fungi, yeast cells, bacilli, cocci, etc., which may lead to some confusion. Blood films taken while making a malaria survey are liable to be vitiated from the air or the human skin; the dirty and sweaty fingers of Indian village children are likely to impose many curiosities on the film.

Fallacies arising from bodies simulating parasites in fresh-blood preparations.—It is specially necessary to acquire a familiarity with the various artefacts occurring in blood films as a result of the physical changes to which red cells are subjected. These can be but briefly alluded to.

Vacuoles in red corpuscles (Fig. 54, *c*; Fig. 55, 6, *e*) are sometimes confusing. They are usually caused by not fixing the film properly or by using greasy

[1] *Internat. Conference on Health Problems in Tropical America*, 1924, pp. 110–17.

[2] *Thirteenth Ann Rep. Med. Dept., United Fruit Coy.*, Boston, Mass., 1924, pp. 213–23. M. A. BARBER and W. H. W. KOMP with the co-operation of H. C. CLARK.

Degenerated and disintegrated leucocytes, with splitting up of the nucleus and vacuolation of the cytoplasm, present at times difficulty in distinguishing them from malaria parasites. They should be studied in detail, keeping in mind the definite characteristics of both asexual parasites and gametes. Very puzzling bodies are bits of leucocytes nipped off or budding; they are bluish like the body of the leucocyte and may have a red granule or so.

Granules of leucocytes resting on red cells are recognised by seeming to vary in size on focusing; they have no amœboid movement, nor the ground-glass appearance of a parasite.

Quinine-affected parasites lack definition in outline and show poor chromatin staining. Mature crescents and often fully developed gametes of benign and quartan parasites do not show any degenerative changes from the effects of quinine, though young ones may.

Particles of pigment from the skin may be mistaken for malarial pigment; the two are easily differentiated; free melanin is very rarely met with—it is either in the parasite or phagocyted; skin pigment is nearly always free, rarely phagocyted. It is, however, impossible to say whether a *single* black granule is *in* or *on* a leucocyte.

Spleen-puncture smears.—In malaria cases with enlarged spleen and anæmia, strange bodies are always seen in films made from spleen-puncture smears Here again, each body whose nature is doubtful should be studied in detail. It is probable that no one can tell what half the bodies seen in a spleen smear are

Estimation of the number of red cells and leucocytes.—The Thoma-Zeiss method is that most commonly used in India. Carefully clean the slide and cover-slip of the hæmocytometer after use; wash them with soap and water and dry them with a clean soft rag.

Variation in the number of leucocytes in malaria.—In malarial fever, in going over the fields of a film one frequently sees that there is evidently an increase in the large mononuclears. This can be verified by a differential count of the leucocytes. This increase is specially marked during the period following the paroxysms, and is, as a rule, absent in the pyrexial stage, during which we may have a leucopenia. "If during a period of low temperature, this change is not found, there is a strong presumption that the case is not malarial. In some cases the change can be detected even during the pyretic period, but in these it is always more marked in the apyretic."[1] This change gradually disappears as convalescence advances. This is a useful test in cases that have been treated by quinine, and one that should be made use of in all doubtful cases where parasites have possibly been missed in the early stage before quinine was administered. The writer has made a series of observations on the effects of quinine in varying doses on different malaria parasites, and has found that even 4 grains a day is in some cases sufficient to eradicate all parasites from the peripheral circulation, and that even 2 grains may considerably reduce their number and alter their appearance, so that in the red cells the young forms look like irregular fragments of blue protoplasm, with fine dots of chromatin scattered through it instead of being limited to the nucleus. An increase beyond 15 per cent. of monocytes (large mononuclears) is considered by STEPHENS and CHRISTOPHERS to be proof of an actual or recent malarial infection, "whereas with a value of 20 per cent. it is almost always possible by long search to find an occasional parasite or pigmented leucocyte. A value of over 20 per cent. probably implies actual infection at the time of observation." "The question of monocytes in modern

[1] STEPHENS and CHRISTOPHERS's *Practical Study of Malaria*, 3rd Ed., p. 43.

tion or a reddish hue. *Hyaline bodies* and " eye-spots " may present some difficulty in distinguishing them from parasites. " They are rounded, oval or spindle-shaped areas devoid of hæmoglobin, and often show a central dot; they do not present the highly refractive appearance of a vacuole. They alter in size on focusing and do not show amœboid movement." They have often been mistaken for new forms of parasites, although they are sometimes seen in perfectly normal blood.

Crenations of red cells are a common cause of mistakes (Fig. 54, *a, b,* and 55, 3). They possess no definite outline; by focusing they will be seen as dark and light points alternately.

Buckled, cupped, folded (Fig. 54, *d, e*) and broken *red cells* may also mislead.

Where whole or fragmented parasites are set free from erythrocytes, they frequently become disc-like or spherical, the cytoplasm appears to become

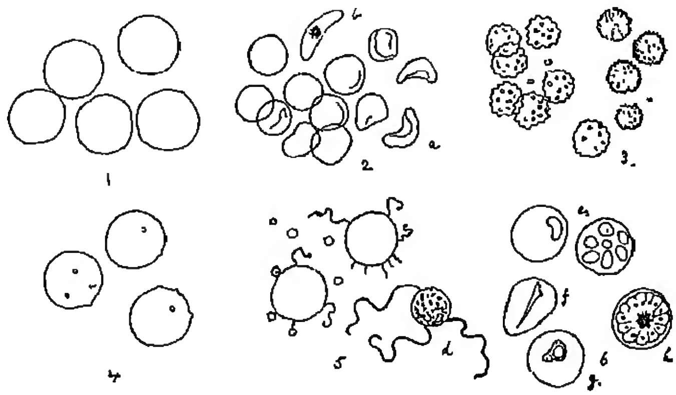


FIG. 55.—1. Thin portion of film. 2. Thicker portion: (*a*) a distorted corpuscle with no pigment; (*b*) a crescent with pigment. 3. Crenated corpuscles. 4. Commencing crenation. 5. (*c*) Red cells with processes; (*d*) a male gamete with flagella and pigment. 6. (*e*) vacuoles; (*f*) a crack, (*g*) a young parasite with very fine pigment; (*h*) a segmenting parasite with central pigment mass.

From STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed.

different, and the hæmozoin is broken up into a number of extremely minute particles showing brownian movement.

Many of the mistakes in connexion with malaria parasites are made with stained preparations. If in doubt it is always advisable to see the living parasite in fresh blood.

Red cells are oxyphilic, that is, they can be stained with acid dyes; hence the great value of the eosin in all Romanowsky stains. Some red cells take up the eosin faintly and are called *shadow cells.* They occur in anæmias and in chronic malaria; in the latter they may be puzzling if we are not acquainted with their nature. In anæmia the red cells may show thread-like processes projecting from the margin after the film has been under observation for some time (Fig. 55, 5, *c*); such cells have been mistaken for microgametes with flagella; here again the entire absence of pigment at once differentiates them from gametes. The processes often break off and float about. Much shorter granular processes are also thrown off by red cells and may be confusing.

II.—General Remarks on Malaria Parasites

Malarial fevers are caused by forms of protozoal organisms which invade the red cells, and gain access to these cells through certain species of anophelines which have previously bitten persons already infected by those organisms. That these parasites are the cause of malarial fever has been proved incontrovertibly. They are always present in the blood at some period of malarial infection. Intravenous injection of malarial blood into healthy persons causes malarial fever in five to ten days, and the same parasites are found in the blood of the injected person. Quinine cures the malarial fever, and at the same time causes the parasite to vanish from the blood.

The malaria parasite in its normal state is a parasite of the red corpuscle, whether endoglobular (intra-corpuscular) or applied to the surface of the red cell. Hence it is well to be on one's guard in diagnosing *free parasites.* They, of course, do occur in the form of spores on the slide (they have been described by different writers on both fresh and stained films), and in the form of free crescents and spherical gametes, but their normal habitat is in association with red cells.

In cases of malarial infection a single 5-grain dose of quinine will sometimes cause all parasites to disappear from the peripheral circulation, a 15-grain dose will very frequently do so. Always inquire, therefore, before examining the blood whether the patient has taken quinine curatively or prophylactically.

In parasites of all species, as growth proceeds, the chromatin scatters through the cytoplasm. When segmentation is about to occur the pigment is gathered towards the centre of the parasite and the chromatin is found in small clumps, forming a definite part of the newly formed segments. At the time of segmentation the chromatin is collected into small masses lying in unstained areas which are the vesicular parts of the nuclei, and these latter are surrounded by thin rings of protoplasm which stain deep blue.

The *crescents of sub-tertian* malaria consist of a large amount of protoplasm and a mass of chromatin packed at the centre or as a loose scattered meshwork—in the female the pigment is in a dense packed mass in the centre; in the male it forms a loose collection generally about the centre, rarely at one of the poles. A narrow line of bright red chromatin can be detected towards the centre of the uniformly light blue flagellum before it is set free from the microgametocyte.

All species of parasites in the first stage of invasion of the corpuscle are ring-shaped, with a small dot of chromatin surrounded by an unstained area, the nucleus, and this again surrounded by a small amount of blue protoplasm.

Fresh preparations are very useful in studying the life-cycle of malaria parasites, but the exact morphological relations can only be demonstrated by staining reactions. Stained preparations are most convenient, especially when films cannot be examined at once.

The vexed question of dried stained films versus fresh preparations is a hardy annual. The writer's opinion is that, for ordinary malarial blood work in the field or in large hospitals where many slides have to be examined, stained preparations are the best. They are indispensable for malarial blood because any other known method produces distortions. Only by dried films can you get the various distinctions of leucocyte granules properly; compare a spleen smear with a spleen section. Dried films may not give the true nuclear characters that the protozoologist gets with Heidenhain's hæmatoxylin stain, *e.g.* in Entamœba, but the protozoologist must produce better results with blood before denouncing dried films.

hæmatology is difficult and has to be re-written" (J. W. W. STEPHENS). This perhaps explains the depreciation of "increase of large mononuclears" of two decades ago as an indication of malarial infection.

Observations on blood examination.—After acquiring a familiarity with the microscopical characters of normal blood, it is well to begin the study of malaria plasmodia on typical cases that have not yet had quinine. The blood of cases of malaria should be examined as soon as they come to hospital and before they have had quinine. Such cases will, of course, be seldom met with in the in-patients of ordinary hospitals. They are best found in the children of bazaars, villages and native quarters generally. If more than an hour is likely to elapse before examining the fresh films, they should be ringed with vaseline and placed in a little slide-holding box, one into which the slides slip edgewise and are kept separate. In films for staining, several completely dried slides may also be carried in a sheet of note-paper, this being so folded that there is a layer of paper between each of them. On the paper opposite each slide should be written any particulars of the case that may be necessary. Without some such device the malaria worker may go on floundering and always be in doubt as to what he sees under the microscope.

Examination of the blood should be carried out in all cases as a routine measure of diagnosis; it will often reveal malaria where it is not expected. "In acute untreated malaria the parasite may be detected practically in every case" (MANSON). The malaria worker must be able to recognise the microscopical appearances of all phases of the malaria parasite in human blood. Practice and intelligent attention overcome the few difficulties met with. *The basis of sound blood work is familiarity with the characters of normal blood*; fresh preparations of malarial blood are best for the beginner.

Best time to find malaria parasites.—The best time for finding parasites in the blood in malarial fevers is from several hours before the beginning of the paroxysm to the time it reaches its height, and again when the temperature has become normal. In India we often meet with negative findings in malarial fevers, especially at the beginning of an infection, even when quinine has not been given. One has every now and then found parasites absent at the first outburst of fresh infections when succeeding paroxysms revealed them. It would be a useful preliminary to the study of human malarial blood to examine the blood of birds known to carry avian malaria parasites. These can always be obtained—for Proteosoma, the sparrow (see p. 117 and Fig. 40, upper line), and for Halteridium (p. 117 and Fig. 40, lower line), the ordinary pigeon. They have this advantage also, that they occur in the blood of these birds throughout the year.

Fresh preparations of malarial blood.—With *fresh cover-slip preparations*, when the parasites are in the form of unpigmented rings, there may be some difficulty in finding them, but in simple tertian and quartan infections, when granules of pigment begin to form early, these are readily recognised, whilst gametes are easier to see in fresh than in stained films, since the pigment in them is very conspicuous, and is often found in a "boiling" state. The sexes are distinguished from the arrangement of the pigment, which contrasts with the colourless protoplasm of the parasite.

Stained preparations of malarial blood.—The *staining reactions* as regards the nucleus and protoplasm are the same in all varieties of malaria parasites. In the Romanowsky stain the nucleus is the only portion of the parasite which takes the chromatin stain; it stains a bright red. Around the nucleus in young forms is always a small amount of protoplasm which stains a delicate blue, and incorporated in the protoplasm is the scanty pigment.

remainder on the first day; in other words, in a high percentage of proved malarial infections parasites were stated to be absent during the first paroxysms. In two Indian battalions quartered in Mandalay, which used to be a very malarious cantonment, six months after the adoption of this change, the place in the returns of practically all the cases of fever of uncertain origin was taken by malaria.[1]

Methods (*a*) and (*b*) will usually be sufficient, and where negative for three consecutive days, malarial infection may well be eliminated. A positive examination, of course, removes the necessity for further observations as regards diagnosis. A film should not be considered negative until 200 fields have been examined: this will, in negative cases, take as a rule seven to ten minutes.[2] It is not sufficiently widely known how uncertain diagnosis by the ordinary thin film may be

When malaria parasites are in sufficient numbers in the blood to give rise to malarial paroxysms, they can in the vast majority of cases be found in the peripheral blood, especially if the thick-film method be employed and quinine be temporarily withheld.

III.—CLASSIFICATION OF MALARIA PARASITES

On the classification, and so on the scientific nomenclature, of human malaria parasites there is no complete agreement. That adopted by STILES and HASSALL[3] is as follows:

Phylum or sub-kingdom PROTOZOA Goldfuss, 1817. Unicellular animals; usually microscopic; free living or parasitic; without true organs

Sub-phylum PLASMODROMA Doflein, 1901. Cilia never present; pseudopodia or flagella present at some stage of the life-cycle; one or more globular nuclei.

Class SPOROZOA. Cell membrane usually present; parasitic and therefore with greatly reduced motility; some show amœboid, some flagellate stages.

Order HÆMOSPORIDIA Doflein, 1901. Without resistant spores in sporocyst. Trophozoite stage intracellular, in blood corpuscles of vertebrates; with change of host (at least in many species); reproduction is an alternation of *x* generations of non-sexual schizogony in the vertebrate host with one generation of the sexual sporogony in a blood-sucking arthropod or a leech.

Family PLASMODIDÆ. Parasite pigmented. Ookinete encysts and forms an oocyst.

Genus *Plasmodium* Marchiafava and Celli, 1885. Gametocytes more or less resemble the schizonts by being round in shape; schizogony in the peripheral blood. *Plasmodium malariæ* Laveran, 1881. Type species *Plasmodium vivax* Grassi and Feletti, 1890.

Genus *Laverania* Grassi and Feletti, 1890. Gametocyte dissimilar from schizont, appearing in form of a crescent; schizogony in red blood cells in internal organs. Type species *Laverania falciparia* Welch, 1897.

The classification here adopted is that the three parasites belong to one genus. The scientific names under this classification are:

1. *Plasmodium vivax* Grassi and Feletti, 1890, for the benign tertian parasite.
2. *Plasmodium malariæ* Laveran, 1881, for the quartan parasite.
3. *Plasmodium falciparum* Welch, 1897, for the malignant tertian parasite. Authors who retain this parasite in a separate genus have till recently called it *Laverania malariæ*. STILES and HASSALL (*l.c.*) have, however, reached the conclusion that the valid specific name, in whichever genus the form is placed, is *falciparum*, a welcome finding in that it simplifies and stabilises nomenclature.

"The malaria parasite, like all true parasites, must be adapted, not only for a life inside its hosts, but also, in order that its continuance as a species may be assured, for a passage from one host to another. Consequently, as regards man, it exhibits two distinct phases—an *intra-corporeal* and an *extra-corporeal*.

[1] Col. P. HEHIR, I.M.S., "Prevention of Malaria in Cantonments in India," *Trans. Internat. Medical Congress*, 1913.

[2] Col P. HEHIR, I.M.S., *Report on Malaria Survey, Burma Division*, 1912, App. I.

[3] "Key-Catalogue of the Protozoa reported for Man," *U.S. Hygienic Lab. Bull.*, No. 140 1925, by C. W. Stiles and Albert Hassall.

On the dried film the name of the person and the date are written with the needle or grease or lead pencil. They may then be stained and examined at once, or kept, after fixing, for months and then stained.

Negative examination of a film does not exclude malaria. Many causes interfere with the finding of parasites, the chief of which is usually the taking of quinine. In military hospitals parasites are found, at the first examination of their films, in 30 to 40 per cent. of actual malaria infections. In the large majority quinine has been given curatively or prophylactically before the film is taken. On stopping the quinine for a few days the parasites appear in a large proportion of the cases previously negative. Negative results are common when the blood is examined during the intervals between one series of paroxysms and another; in all probability parasites are present, but are too few to be found by the procedure used—as is indicated by the greater number of positive results obtained with thick films of malarial blood. In initial paroxysms we may fail to find parasites in the examination of a single thin film.

Few parasites in the cutaneous blood may yet be associated with a heavy infection, and may be connected with dangerous symptoms, especially in cerebral sub-tertian malaria. Sometimes the rings are late in appearing, hence the value of making two-hourly examinations in cases where the first examination is negative, and of examining stained thick films.

Malaria parasites may be present in the blood, but not be discoverable by ordinary blood examinations. ACTON, RENNIE and their colleagues in the Dagshai Malaria Depot (where re-infections did not occur) have shown in a series of observations that negative examinations were frequent in persons whose blood subsequently contained parasites. In one series they record 564 negative examinations in 82 persons in whose blood the benign tertian parasite subsequently appeared. The writer has recorded a similar series (*vide infra*). The thin film is not an infallible guide in the diagnosis of malaria. This is well recognised by those who use provocatives to shed parasites into the cutaneous circulation, and also in the use of the thick film. Thick and thin films from numerous patients were each examined for five minutes. In one series thick films were positive in 526 cases, whereas of the corresponding thin films only 125 were positive. In another series of 1,431 thick and thin films, taken in each case on the same slide from malaria cases, the thick film gave 45·8 per cent. positive, and the thin film only 17·5 per cent.

The writer would quote another group of observations in support of this statement which he had carried out. In the Burma Division, up to October, 1911, a large percentage of "fever" cases were returned as pyrexia of uncertain origin, the practice being to rely upon a single examination of a stained blood-smear for malaria parasites. From that month onwards, daily microscopical examinations of the blood in all cases of undiagnosed pyrexia were carried out, quinine being withheld until malaria parasites were found in the peripheral blood. Over 9,000 slides were examined in connexion with 715 infections In collecting the data for the above-mentioned investigation, a blood examination for malaria parasites consisted of the following procedure carried out on three consecutive days:

(*a*) Examination of two fresh films.
(*b*) Examination of two stained smears.
(*c*) Examination of a stained thick film.
(*d*) Examination for pigmented leucocytes.
(*e*) A large mononuclear count.

In one case parasites were not found until the eighth day, in two on the seventh day, in five on the sixth day, in four on the fifth day, in eleven on the fourth day, in forty-three on the third day, in 127 on the second day, the

follows the parasite is considered as holding this position. In many stained preparations we find that an occasional parasite seems as if it were simply attached to the surface of the red cell, it is considered that these attached parasites were unable to penetrate the red cell; "the number of such individuals increasing in an old infection" being due possibly to decreased power in the merozoites themselves, or to increasing resistance of the red cells, or possibly to both these causes combined.[1] There is no doubt that both asexual and sexual forms can and do develop to maturity—when attached to the surface of red cells in the manner stated.

The discussion, however, is academic, largely because the structure of the red cell is not fully known. Has a red cell got an "inside"? The important point is that, whether the parasite is in or on the red cell, the cell is destroyed.

M. ROWLEY-LAWSON is also of opinion that crescents are always extracellular. Prof. J. W. W. STEPHENS and R. M. GORDON[2] have advanced a similar view with regard to crescents and have given some figures in four plates in the paper referred to which are convincing as to an extra-corporeal habitat of some of the crescents. LAVERAN, ARGUTINSKY, PANICHI and others hold the view that human malaria parasites are not endoglobular, but adhere to the surface of the red cell.

J. A. SINTON,[3] by crenating erythrocytes with hypertonic, and ballooning them with hypotonic, saline believes that he has seen parasites in the various extra-corpuscular positions named by ROWLEY-LAWSON.

The life-cycle of malaria parasites.—As was made clear when considering the zoological classification of *Plasmodium*, the species has a life-cycle in two hosts. The sexual syngamy takes place in the stomach of a female anopheles, which is accordingly the *definitive* host, and which has sucked the sexual elements or gametocytes from the blood of man. The final products of conjugation, after a complicated development (sporogony), are injected by the mosquito at a subsequent feed into man, in whom an asexual cycle (schizogony) is instituted and indefinitely repeated. No resistant spores are developed in the mosquito, the sporozoites not being enclosed in any capsule or envelope. Man is then the *intermediate* host, in whom, too, gametocytes form, ready to produce syngamy if ingested by an Anopheles.

The malaria organisms are, then, obligatory parasites throughout their life-cycle. They have no free stage. Without a host they die inevitably.

Asexual schizogony in the blood of man.—(Fig. 56.) The Plasmodium is parasitic in, or as some hold on, the red blood corpuscle. The youngest form is an undefined, pale amœboid disc in which pigment, derived from the hæmoglobin, shortly appears. This, as growth proceeds, increases and aggregates, the particles being of different size and colour in different species, and collects towards the centre of the parasite, whose peripheral part segments into spores, which, by rupture of the red cell, are discharged into the plasma and attack other red cells if not previously destroyed.

"In stained specimens the small Plasmodium consists of a deeply tinted chromatic mass, a vesicular nucleus and a lightly tinted covering of protoplasm. As it grows and nears full development the nucleolus increases in size, is less defined, and then disperses. Lastly, just before sporulation both nucleus and nucleolus cease to be distinguishable, becoming fragmented and diffused throughout the protoplasm. Then the nuclear elements reappear as numerous minute scattered nucleoli, and it is around these that the protoplasm of the segmenting parasite arranges itself to form the spores. The vesicular character of the nucleus does not usually appear in these until after they have become free in the liquor sanguinis. Until the pigment is concentrated it is scattered

[1] J. D. THOMSON and H. M. WOODCOCK in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. II, p. 1523.

[2] *Annals of Tropical Medicine and Parasitology*, Vol XVIII, No. 1, April 30, 1924, pp. 33–35.

[3] *Ind. Med. Gaz.*, October, 1922, pp. 367–71.

Clinical observation and analogy alike make it certain that there is yet another phase, also intra-corporeal—the latent phase whose characters as yet can only be conjectured " (MANSON).[1]

Mixed infections.—These are by no means infrequent, the commonest being that of malignant tertian and benign tertian. A remarkable case of mixed infection is recorded by Lt.-Col. C. DONOVAN, I.M.S., in the *Report of the General Hospital of Madras* for 1907. The patient, a wandering mendicant, was admitted for fever, and all the species of malaria parasites were present in his blood—*Plasmodium malariæ* predominated, *P. falciparum* next, with only a few *P. vivax*. A single dose of quinine was given, the temperature became normal and remained so for nineteen days; it then rose once more, the rise being associated with crowds of schizonts of *Plasmodium vivax*, but neither of the other two species. Another dose of 30 grains of quinine was given and after thirty-six days of freedom from fever a second relapse occurred, and on this occasion only *P. falciparum* was found in the blood. When only one type of parasite is found on the film it is not possible to state from the film alone that there may not be another type of parasite somewhere in the body. In the majority of mixed infections one of the co-existing parasites for the time being plays the dominant rôle and may temporarily suppress the other.

Simultaneous sporulation of parasites.—In all forms of malarial fever the liberation of swarms of spores usually coincides with the onset of the attack of fever, the fever being probably due to the setting free, at the time of the rupture of the corpuscles, of toxins which possess heat-producing (pyrogenetic, thermogenetic) and red-corpuscle-destroying (hæmolytic) properties.

Malaria parasites, like all Protozoa, are unicellular animal organisms; like all Sporozoa, they are without organs of locomotion, they reproduce by sporulation, and are parasitic. Among the Sporozoa simple non-sexual division cannot be carried on indefinitely; to effect this a sexual cycle must be introduced, and in the case of malaria parasites this cannot be effected whilst the parasite is still in the human body. So far as we know at present, this can only be brought about through the medium of certain species of anophelines. In the human body the malaria parasite tends to exhaust its powers of multiplication, and if the patient has been able to battle against its ravages, he recovers. The parasite cannot pass naturally from one man's blood to another's except through anophelines.

Is the malaria parasite intra-corpuscular or extra-corpuscular.—In the foregoing remarks on malaria parasites it has been assumed that in the blood the parasites are intra-corpuscular. The great majority of malariologists believe that the parasites develop *inside* the red cells, but some of the highest authorities have in the last few years brought forward evidence that at least calls for a reconsideration of this question.

M. ROWLEY-LAWSON holds the opinion that each individual parasite, during its growth, infects and destroys several red cells, detaching itself from the infected cells one after another. She bases this view mainly on the fact of having frequently met with growing forms of the parasite free in the blood. In carefully made smears free parasites are rarely seen. The actual changes that take place in infected red cells —enlargement, discoloration, etc.—take place concurrently with the development of the parasites. " In certain chronic cases the parasites may remain attached to the corpuscle and successfully complete their development, so far as can be seen, in this extracellular position; this applies both to the asexual and sexual forms."[2] The writer considers that the vast majority of parasites are intracellular, and in what

[1] *Tropical Diseases*, 7th Ed., p. 4.

[2] J. D THOMSON and H M. WOODCOCK in BYAM and ARCHIBALD's *Practice of Medicine in the Tropics*, Vol. II, p. 1521

it may be due to the stain. Do not attach undue significance to the size of the red cell—some are normally large. In *quartan* infection the infected cell retains its normal colour and size, or may become smaller. In *simple tertian* the infected red cell increases considerably in size, becomes paler, and otherwise changes. The effect of *sub-tertian* parasites on the size of red cells may vary; at times they are diminished, but mostly they are unaffected or only slightly increased; sometimes they are irregular or crenated, and the colour may be heightened or lessened.

Characters of the pigment.—The pigment of malaria parasites may occur in very fine dust-like particles, or as large granules, thin lines, fine needles, or grains. In recent infections it is found as minute grains; in longer infections as coarse particles or collected into irregular lumps. The largest needles or lines of pigment are not more than 1 μ in length; when they run together the pigment granules and lines form clumps. When in larger masses the pigment is brownish black; when in fine lines, needles or granules it is reddish brown. The parasite lives in and devours the red cell. It metabolises pigment from it. The excreta of the parasite remain in the cell until the cell bursts, when hæmozoin [1] is discharged into the blood. The pigment appears early in intracellular life, and when present, renders it easy to see the parasite in fresh blood. The size of the granules of pigment varies in the different species of parasite. As the pigment is disposed in the protoplasm of the parasites, it shares with them the amœboid movement when the parasites are still living. "In addition the pigment shows a second communicated movement which is most marked in the adult sexual forms of the parasites. This consists in a more or less to-and-fro wavering of the pigment elements. When slight the pigment granules move sluggishly, scarcely changing their place, but when marked they whirl about like a swarm of midges" (MANNABERG).[2] This last is the so-called "boiling" or *bubbling movement* of the pigment.

Malaria pigment is unaffected by strong mineral acids, but it is affected by weak alkalis, and then acquires a yellowish or reddish brown colour. It is entirely and quickly dissolved by ammonium sulphide, and it is altered by potash. It does not give the blue reaction of iron with ferrocyanide of potassium. "It is an iron-containing derivative of hæmoglobin which is primarily split up into protein-globulin and a pigment-hæmatin, and it is from the latter that the hæmozoin is derived."

The pigment in quartan is chocolate-coloured, seen as comparatively large brown granules mixed with small reddish ones. In simple tertian the pigment is more straw-coloured, faint pale ochre colour or greenish, and the granules very small. In the unstained specimen of the quartan parasite there is a small dot in the centre which is the nucleus and is often visible; it is not pigment.

Chromatin.—Simple or multiple, deeply or faintly stained; its extent, amount and distribution should be noted.

Size of the parasites.—In the different phases of their development the malaria parasites vary from 1 to 10 μ in diameter, the first representing the smallest rings of malignant tertian, the latter the full-grown parasites of quartan and the different forms of gametes; the fully grown benign tertian, however, frequently has a diameter of 16 μ.

Gametes.—The ordinary dimensions of a full-grown crescent are 8 to

[1] *Hæmozoin* is the term given by SAMBON to malarial melanin. The term *black pigment* is inappropriate, indefinite, and inaccurate, as the colouring matter is never actually black in human malaria, it varies from yellow to brownish black.

[2] *The Malarial Parasites*, New Sydenham Society's Translation, p. 293.

throughout the parasite, but mostly in the outer zone Apparently so long as the nucleus remains entire, the hæmozoin is peripheral; when segmentation occurs in the nucleus the hæmozoin becomes central."[1]

Development of asexual malaria parasites in the blood—endoglobular cycle or schizogony.—This is similar in all essentials in the three species of malaria parasites, each, however, having its own characteristics.

Schizogony is easily studied in the benign tertian forms of malarial infection as the plasmodia are in the peripheral circulation; the same holds good with quartan, but the cycle is spread over a longer period. In the unstained specimen of the quartan parasite there is a small dot in the centre which is the nucleus and is often visible. In *P. falciparum* schizogony cannot be studied, as it goes on in the internal organs; multiplication of the nucleus of the schizont commences by a primitive form of mitosis, but as the nuclei increase in number the method of development is that of a type of multiple nuclear fission (SCHAUDINN); very occasionally a fully developed schizont is seen in peripheral blood.

IV.—DESCRIPTION OF MALARIA PARASITES

The parasite is a microscopic mass of protoplasm containing a nucleus; it has no definite organs of locomotion or digestion, its body-protoplasm is very irritable, moves by amœboid activity, assimilates nutriment, grows, divides and produces by metabolic and chemical processes a variety of chemical compounds, some of which are toxins and are believed to cause the malarial paroxysms from which the infected person suffers.

Points to observe in malaria blood films.—The different points to observe in determining the species of malaria parasite present are stages of the parasites met with in the peripheral blood; character of amœboid movement in the Plasmodia; presence or absence of pseudopodia; effects of the parasites on the erythrocytes; dimensions of the parasites; number of merozoites; duration of the asexual cycle; sites of sporulation; presence or absence of sexual forms, and if present, their shape and characters; and character of the pigment.

Amœboid movement of parasites.—*Amœboid movement* is most active and continues longest in simple tertian parasites (hence the name, *vivax*, lively); in quartan parasites it is sluggish but visible; in *sub-tertian* very lively in the youngest unpigmented stage. In all forms the movement slows down as the intra-corpuscular parasite acquires its full size. In all species the young forms are so perpetually changing their shape that they are difficult to describe. Only after death do they have a constant shape, usually that of a ring form, or, occasionally, a disc shape. Crescents possess no amœboid motion, but have the power of gradually changing their shape.

Multiple infection of red cells.—It frequently happens in severe infections, especially of malignant tertians, that two or even three or more parasites occupy a single red cell. The writer has several times seen five malignant tertian rings in one red cell. In heavy infections 50 per cent. of the red cells may be attacked, though this is uncommon. The co-existence of a developing schizont and a gamete, or of two gametes, in the same red cell is sometimes very puzzling.

Effect on red cells.—Note any stippling, fine and diffuse (Schüffner's dots), or very coarse, few and irregular (Maurer's clefts[2]). Do not mistake very early Schüffner's dots made conspicuous by deep staining and partial hæmolysis of the film for Maurer's clefts. Absence of stippling is of no importance;

[1] MANSON'S *Tropical Diseases*, 8th Ed., pp. 10, 11. [2] See footnote p. 168.

Comparison of Developmental Processes in Malaria Parasites with Protozoa Generally

Scientific terms.	Description	Terms commonly used in describing the development of malaria parasites
Schizogony	The asexual or endogenous cycle.	Cycle in man.
Schizont	The parasite of the asexual cycle, segmenting or rosette body.	Sporocytes.
Merozoite (spore)	The young parasites resulting from asexual division.	Spores.
Gametocyte	Potentially sexual forms.	Gametocyte—crescents in malignant tertian and spherical gametes in quartan and benign tertian.
Microgametocyte	The male form.	
Macrogametocyte	The female form.	
Gametogony	Sexual cycle which is noted in the surface blood from ring to gametocyte.	
Microgamete	The fertilising element or elements, "spermatozoa" discharged from the male gametocyte.	Flagellum or microgamete.
Macrogamete	The female sexual form after extrusion of polar bodies (maturation).	Macrogamete.
Syngamy	Fertilisation of the female gamete by flagellum.	
Sporogony	The sexual or exogenous cycle.	Cycle in mosquito.
Sporont or zygote	The fertilised female.	
Ookinete	The motile fertilised macrogamete.	Travelling vermicule.
Oocyst	The encysted ookinete. The non-motile fertilised macrogamete, applied whether originally motile or not.	Zygote.
Sporoblast	The primary division of the protoplasm of the oocyst (zygote).	Blastophore; sporoblast.
Sporozoite	The final product of the sexual development formed from the sporoblasts or blastophores.	Zygotoblasts, blasts, or sporozoites.
Trophozoites	Any stage of the intra-corpuscular asexual stages of the parasite.	
Endogenous cycle	Development of gametes in the red cells.	

cyte-containing blood is made upon a thin slide (1 mm. in thickness, so as to be easily focused through a $\frac{1}{6}$-inch lens). The wet film should be breathed upon and then placed face downwards upon a second slide covered with a small piece of damp filter paper in the centre of which a small opening is cut. The two slides are bound together by means of elastic bands, thus forming a tightly sealed damp chamber. The ex-flagellation of the crescent can now be observed under the microscope, and immediately this occurs the film is dried and stained in the ordinary way."[1] By this method the living parasite may be watched through a $\frac{1}{8}$-inch objective in the moist chamber and fixed at the right moment.

The following is also a satisfactory method. Select a gametocyte carrier. Take a thick piece of blotting paper and cut eight holes in it, each about $\frac{1}{2}$ inch square. Moisten the blotting paper and place it on a flat surface. It makes a series of moist chambers. Prick the patient's finger. Take the slide and breathe on it. Take a small drop of the patient's blood on the slide and spread it out with a needle and place the slide face downwards with the drop of blood over one of the holes in the blotting paper. Do this for eight slides. At

[1] MANSON'S *Tropical Diseases*, 8th Ed., pp. 826, 827.

10 μ (sometimes, however, reaching 15 μ) long and 2 to 3 μ broad about the middle.

Regarding *gametes*, note the degree to which the protoplasm stains—dark blue in the macrogamete, light blue in the microgametocyte; appearance of chromatin, extent, arrangement, degree to which it stains; appearance of pigment, its arrangement and degree of coarseness.

The chromatin in parasites that are to develop to gametocytes undergoes definite changes. The first stage is, as in the young schizont, a solid block. It subsequently divides into two separate granules, but does not become diffused throughout the protoplasm as it does in the schizont. In the full-grown gametocyte the chromatin, composed of numerous particles packed together, forms one mass in the interior of the parasite, surrounded by a zone free from pigment and staining feebly.[1]

Site selected for sporulation.—This is important. *Plasmodium falciparum* sporulates almost exclusively in internal organs, and the serious clinical manifestations which sometimes occur in this infection arise from sporulation in the brain or other vital organ. Sporulation of *P. vivax* takes place largely in the spleen and bone marrow, but occasionally in the circulating blood; that of the quartan parasite occurs in the general and peripheral circulation and scarcely, if at all, in internal organs.

Vitality.—Asexual malaria parasites appear to possess extraordinary vitality. The sterile fluid from defibrinated malarial blood can be kept in ice and remain infective for at least sixty-five hours; the parasites stain well after being in the ice-chest for seven days.[2]

Search for parasites in a film: stained preparations.—Examine red cells. Parasites are definite and unmistakable organisms with a characteristic structure. "Nothing that is at all indefinite is likely to be a malarial parasite" (S. P. JAMES). The stained malaria parasite in a red cell is perfectly distinct and visible at once. The ring forms are specially characteristic; the brilliant red dot of nuclear chromatin at one point of the periphery is unequivocal. Around the red dot or adjacent to it is an oval or circular clear area like a vacuole, and surrounding this area is the blue protoplasm of the body of the parasite.

The terms used in connection with the various stages of the development of malaria parasites and protozoa are given in the Table on p. 160.

The sexual cycle.—(Fig. 56.) If the female Anopheles imbibe both male and female mature gametocytes the following changes occur. The microgametocyte becomes spherical if not already so, the protoplasm undergoes "boiling" and flagella appear and are detached, forming the male or impregnating gamete. One of these, and one only, enters the macrogamete. The zygote results, and becomes oval, elongate, lanceolate, vermiform, the oökinete; this penetrates the stomach wall and grows into the oöcyst; the contents of the oocyst subdivide into cytoplasmic masses, and on the surface of these there form the elongated sporozoites, of which it is estimated that 10,000 may be present in a single oocyst. The rupture of the oocyst throws these into the body cavity, whence they are carried as a veritable septicæmic-like condition to all parts. Those which reach the salivary glands are injected with the poison when the female Anopheles next feeds and so re-enter man, to take up again the schizogonic cycle.

Method of staining the flagellated body in malaria.—There are several methods. For work in India McKAY's is the best. "A thin film of gameto-

[1] DANIELS and NEWHAM, *Laboratory Studies in Tropical Medicine*, 5th Ed., pp. 128, 129.
[2] H. M. CLARK, *Brit. Med Jl.*, March 28, 1925, p 600.

and wriggle over the field with such rapidity as to be difficult, usually, indeed, impossible to follow.

The process of ex-flagellation of male gametocytes and the extrusion of "polar bodies" from the female is best studied in an unstained preparation of fresh blood. In making the observation lower the condenser and partially close the diaphragm.

Specially made preparations show many well-stained flagellated bodies, spherical bodies, and still some crescents. If the cover-slips are removed and dried, in five or ten minutes only crescents, ovals and spheres are found. If left three-quarters of an hour free microgametes and residual masses are seen; some of the latter possibly in phagocytes. Sometimes flagellated bodies are seen to be contained in phagocytes. Carbol-fuchsin staining gives elegant preparations, but does not, of course, display the chromatin, for this, one or other of the Romanowsky stains is required.

The flagella, which vary in number from one to six from each microgamete, are extremely delicate filaments which vibrate rapidly and are never seen in fresh blood just removed, but only after it has been exposed to air some minutes.

In India there are, as far as we at present know, only three forms of malaria parasites, giving rise to the three forms of malarial fever met with.

Quartan Parasite

Quartan ague is due to *Plasmodium malariæ* (Plate XI, Figs. 58–75). The life-cycle of this parasite lasts seventy-two hours. Two or more generations of the parasite may carry on their life-cycle in the blood simultaneously, giving rise to double or triple quartan ague

The young parasites usually have the signet-ring character (Plate XI, Fig. 58) and are difficult to distinguish from *P. vivax*. The rings are compact; pigment appears early. The developing schizont is only slightly amœboid, and for this reason we do not see so many irregular forms in stained preparations as there are in benign tertian slides. The vacuole, present in the earliest stage, soon disappears. The half-grown schizont is often seen to form an equatorial band across the erythrocyte (Plate XI, Figs. 61, 62), later on it is more or less rhomboidal, the nucleus being elongated. The red cell does not enlarge, the tendency is for it to contract; it remains round and stains differently from the uninfected surrounding cells; at any rate, there are rather distinct changes in the red cell, but it is difficult to define them. Schüffner's dots are absent. The pigment is of a darker brown than that of *P. vivax*, and the rods and granules are coarser, they tend towards the periphery of the parasite. The pigment is not moved about in the same rapid way as in *P. vivax*. There is sometimes delay in the splitting up of the chromatin, which may lead to the asexual parasites being mistaken for gametes. The fully developed schizont (Plate XI, Fig. 68) is conspicuously smaller than that of *P. vivax*, being usually 6·5 μ in diameter; it therefore does not fill the red cell. There is a rich development of chromatin. Nuclear division (Plate XI, Figs. 64–68) may begin after the schizont has been growing for forty-eight hours, the division being slow. It produces six to twelve merozoites, eight or nine being the average (Plate XI, Figs. 69, 70); the arrangement is distinctly daisy-like, the spores being regularly grouped about the margin of the red cell The individual merozoites are somewhat larger than those of *P. vivax*. The pigment is collected into two or three small groups or masses.

Plate IX, Fig. 1, shows *Plasmodium malariæ* in fresh unstained blood:

intervals of five minutes take up the slide, dry it and stain with Leishman. In the hot weather ex-flagellation takes place in a few minutes, in the cold weather in about half an hour (S. R. CHRISTOPHERS).

Ex-flagellation.—When ex-flagellation is about to take place the whole microgametocyte vibrates and oscillates. The vigour with which the flagella move is often seen to be sufficient to cause deep indentations in the red cells, which, however, are only momentary, as the elasticity of the red cells enables them to recover their normal shape at once. The movements of the flagella continue as a rule for from twenty to thirty minutes, but may occasionally be seen after even two hours. In their most active condition the individual flagella cannot be recognised, since their movements are quicker than the eye can follow; as the movements become weaker they are seen distinctly; they

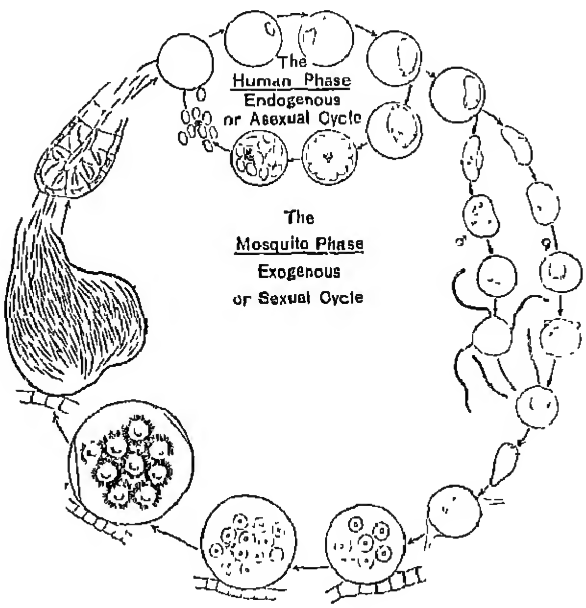
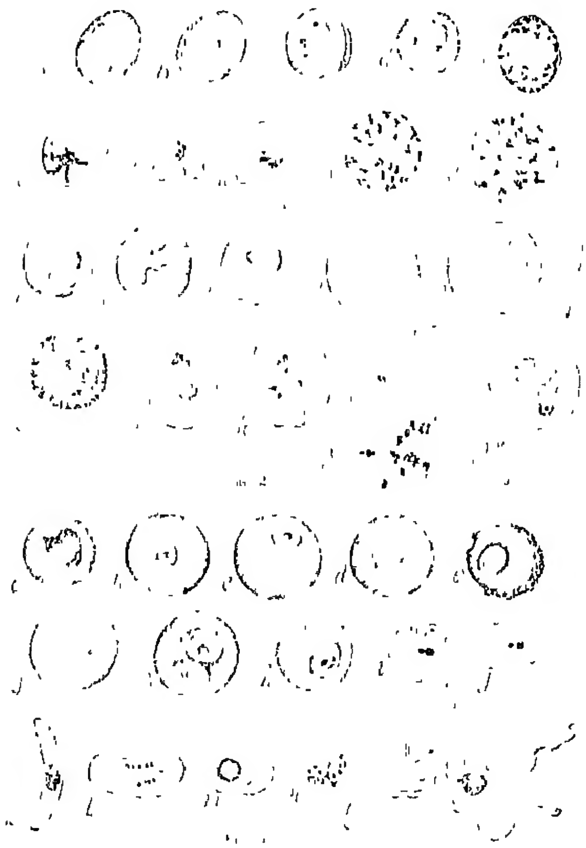


FIG. 56.—Diagram of the Asexual and Sexual Cycles of the Malaria Parasite. From DANIELS and NEWHAM'S *Laboratory Studies in Tropical Medicine*, 5th Ed.

then become more intermittent and eventually cease. At this stage the flagella that have not broken away are seen to be attached to the body-protoplasm of the microgametocyte. The flagella are from two to four times the diameter of a red cell in length. The movements of detached flagella are very similar to those of an eel in water or a snake along the ground; they are usually of a lashing character, and in fresh films are seen to agitate the red cells violently. They are difficult to follow in their wanderings amongst the red cells.

In stained ex-flagellation preparations we often find flagella lying just within the periphery of the gametocyte. In fresh preparations a flagellum can sometimes be seen in a state of great agitation within, repeatedly thrusting itself against the limiting membrane which it bulges, and we may occasionally see it actually burst through and commence moving outside the spherical body, to which, however, it is still attached; and later see it become detached

PLATE IX



MALARIA PARASITES IN FRESH BLOOD.

FIG. 1.—Parasite of quartan infection.

FIG. 2.—Parasite of benign tertian infection.

FIG. 3.—Parasite of sub-tertian infection ("æstivo-autumnal"). (*Compiled from* THAYER *and* HEWETSON.)

(From MANSON'S *Tropical Diseases*, 4th Ed.)

shape and almost completely hides the containing red cell; the pigment grains are numerous, coarse, scattered and conspicuous.

Simple Tertian Parasite

Simple tertian or benign ague is due to *Plasmodium vivax* (Plate X, 1–37). The life-cycle of the parasite is forty-eight hours. Two generations of the parasite may in simple tertian also carry on their life-cycles simultaneously, giving rise to double tertian ague.

The diameter of the ring is from 2·5 to 3 μ, though a large one may reach 3·5 to 4 μ. The nucleus is, as a rule, a single, comparatively large granule, but it may be semi-circular, rod-shaped or crescentic, or rarely ring-shaped (Plate X, 7–12). It may appear to be separate from the cytoplasm, being apparently in the vacuole itself (Plate X, 8, 9), but it is probably in the cytoplasm of the upper or lower surface of the sphere. A vacuole forms rapidly in the cytoplasm, and soon becomes large compared with the ring of protoplasm. One side of the ring is often thicker than the other. The nucleus forms a conspicuous granule situated usually in the thinner part of the ring (Plate X, 5, 6, 12). Hence the well-known signet-ring appearance of the young growing parasite. The large vacuole has a nutritive function. The trophozoite may assume many shapes and the ring form of *P. vivax* shows, at an early stage, great activity and alteration of shape, rendering it irregular or even angular (Plate X, 13–15), and in some the cytoplasm will be seen to be throwing out pseudopodia (Plate X, 15). Multiple infections of single red cells are common in relapses and chronic malarial infection—two or three, or even five or six rings being found in a single cell (Plate X, 10–12). This is seldom seen in the primary infections of non-epidemic years. The parasite rapidly increases in size for about forty hours, and then attains its mature dimensions. Throughout this time it shows active amœboid movement, throwing out pseudopodia in various directions. Therefore in fixed stained preparations all possible variations in shape are met with (Plate X, 17–21).

Plate IX, Fig. 2, shows *Plasmodium vivax* in fresh unstained blood. *a*, Early stage of the benign tertian parasite. Seen as a small pale speck on or in the invaded red cell, and much like the corresponding stage of the quartan, but differs from it in exhibiting very much greater amœboid activity, changing its form and location in the corpuscle incessantly. *b*, Pseudopodia which are pushed out and retracted rapidly. This activity continues during the growth and formation of the hæmozoin though in a progressively diminishing degree. *c*, *d*, *e*, Show the rapidly changing irregularities in the contour of the parasite which occur; these changes are suspended by the time hæmozoin-concentration is effected. *f*, The particles of hæmozoin are seen to be finer than those of *P. malariæ* and are in a state of much more active and incessant movement, constantly changing their position in the peripheral region of the erythrocyte in which they, for the most part, seem to lie. *d*, *e*, *f*, *g*, Also show the enlargement (often to twice the normal size) and marked decolorisation of the red cell containing the parasite. *h*, Segmenting parasite resembling a cluster of grapes in some more or less central part of which one or two masses of dark pigment have accumulated among the berries. The spores, arranged in what is called the "rosette" form, fifteen to twenty-six in number, are smaller, smoother and more spherical than those of the quartan parasite; nuclei are rarely to be seen. *i*, The separating spores. *j*, Flagellated (spherical) male gametocyte.

Effects on the red cell.—As the trophozoite enlarges, great changes occur in the red cell. It increases in size and gradually becomes paler as it expands

a, earliest stage in red cell. At this stage of unpigmented life the quartan parasite takes on the form of a small, roundish, clear speck, showing up somewhat indistinctly against the hæmoglobin of the invaded corpuscle, and amœboid action is feeble. *b, c, d, e, f,* Stages in the growth, maturation and sporulation of the quartan parasite. As soon as the parasite becomes pigmented all amœboid movement ceases. Note that relatively to other malaria parasites the hæmozoin carried by the quartan is large in amount, coarse in grain, sometimes forming short rods. *g, h,* Segmented or mature parasite made up of eight to ten spores arranged daisy fashion very symmetrically around the now centrally placed massive block of brownish black hæmozoin. About the centre of each spore a shining nucleolus can usually be made out readily. *i,* Male gametocyte;

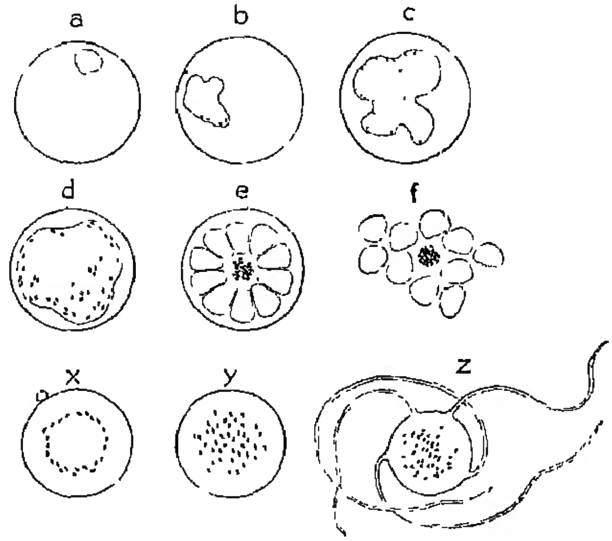


FIG. 57.—*a* to *f*, Phases in the asexual development of the quartan parasite; *x* to *z*, phases in the sexual development of the same parasite.

From DANIELS and NEWHAM'S *Laboratory Studies in Tropical Diseases*, 5th Ed.

a spherical pigmented body looking like an ordinary large pigmented parasite that has escaped from a red cell It may occasionally be recognised as a gamete by the very active movement of the hæmozoin granules, although this only occurs during the pyrexial stage of the paroxysm.

Quartan gametocytes.—The development of the sexual forms of *P. malariæ* is much the same as that of *P. vivax*. In the growing state they have some resemblance to developing schizonts, as these show little amœboid movement. The young macrogamete has more pigment and less chromatin than the schizont of corresponding size; the male has a larger amount of chromatin and its protoplasm stains less deeply. Adult gametocytes are seldom met with in large numbers, except in heavy infections in areas where quartan malaria is the predominating form of infection. In other regions they are not only scanty but are often absent from the peripheral blood. They are in almost every respect similar to those of benign tertian, except that they are smaller. The *male* is about the size of a red cell, and is readily distinguished (Plate XI, Figs. 71, 72); the *female* (Plate XI, Figs. 73, 74) tends to assume an ovoid

PLATE X[1]

ENDOGENOUS CYCLE OF PLASMODIUM VIVAX IN THE BLOOD

Figs 1 and 2 Merozoites which have attached themselves to, but have not yet penetrated, the red cell.

" 3 and 4. Young parasites in the act of penetrating

" 5–16. Various appearances of the ring form and early stages of the young trophozoite. Fig 6, early stippling, and Fig. 11, punctate basophilia of the host-cell. Figs 10 and 11, double infection, and Fig. 12, triple infection of the cell.

" 17–21. Intermediate stages in the growth of the schizont, showing the bizarre appearances assumed by some of the parasites when amœboid activity is at its height. Schuffner's dots are well marked, now and onwards, in the host-cells.

" 22 and 23. Adult schizonts.

" 24–30. Stages in schizogony up to the separation of the merozoites and their liberation from the host-cell

" 31 and 32. Mature male gametocytes.

" 33–35 Growing female gametocytes. The absence of a vacuole and of pseudopodial processes is to be noted.

" 36 and 37. Mature female gametocytes.

[1] From J. D. THOMSON and H. M. WOODCOCK's article, "The Parasites of Malaria," in BYAM and ARCHIBALD's *Practice of Medicine in the Tropics*, Vol. II.

PLATE XI[1]

LESS COMMON APPEARANCES OF PLASMODIUM VIVAX (AND OF P. FALCIPARUM); MATURATION PHASES, AND SPECIAL FORM OF P. VIVAX; ENDOGENOUS CYCLE OF P. MALARIÆ

Figs. 38 to 42. *P. vivax* in advanced stages of development, apparently attached to the outside of the cells (from an old relapsing case) Figs 38 and 39, developing gametocytes, 40–42, schizonts undergoing schizogony.

,, 43–49. Various "combinations" of two parasites, which have grown up and reached maturity together in the same cell Figs. 43–47 relate to *P. vivax* Fig 43, schizont *plus* schizont, both segmenting; 44, segmenting schizont *plus* male gametocyte; 45 and 46, segmenting schizont *plus* female gametocyte (schizogony of "macrogamete" according to Schaudinn's theory); 47, female gametocyte *plus* female gametocyte. Figs. 48 and 49 relate to *Plasmodium falciparum*; 48, schizont *plus* schizont, both segmenting. 49, gametocyte *plus* female gametocyte.

,, 50–53 Stages in the elimination of chromatin from the nucleus of ripe gametocytes (of *P vivax*), which has taken place during the interval between drawing the blood and drying the film in air. Fig 50, deeply staining superfluous chromatin being separated from the paler staining nucleus (pronucleus) Figs. 51–53, the superfluous chromatin extruded at the surface, in the form of "polar bodies"

,, 54–57. Hitherto undescribed form or phase of *P. vivax* (J D. Thomson and H. M Woodcock).

,, 58–75. Endogenous cycle of *P. malariæ*

,, 58. Ring form.

,, 59 and 60. Young growing trophozoites.

,, 61 and 62 Characteristic band forms of the schizont.

,, 63. Adult schizont. (Note, throughout, the small size of the host cell and the absence of Schuffner's dots.)

,, 64–70. Stages in schizogony up to the separation of the merozoites inside the cell

,, 71 and 72. Mature male gametocytes

,, 73 and 74 Mature female gametocytes.

,, 75. First stage in the maturation of a female gametocyte.

[1] From J D Thomson and H. M Woodcock's article, "The Parasites of Malaria," in Byam and Archibald's *Practice of Medicine in the Tropics*, Vol. II

PLATE X

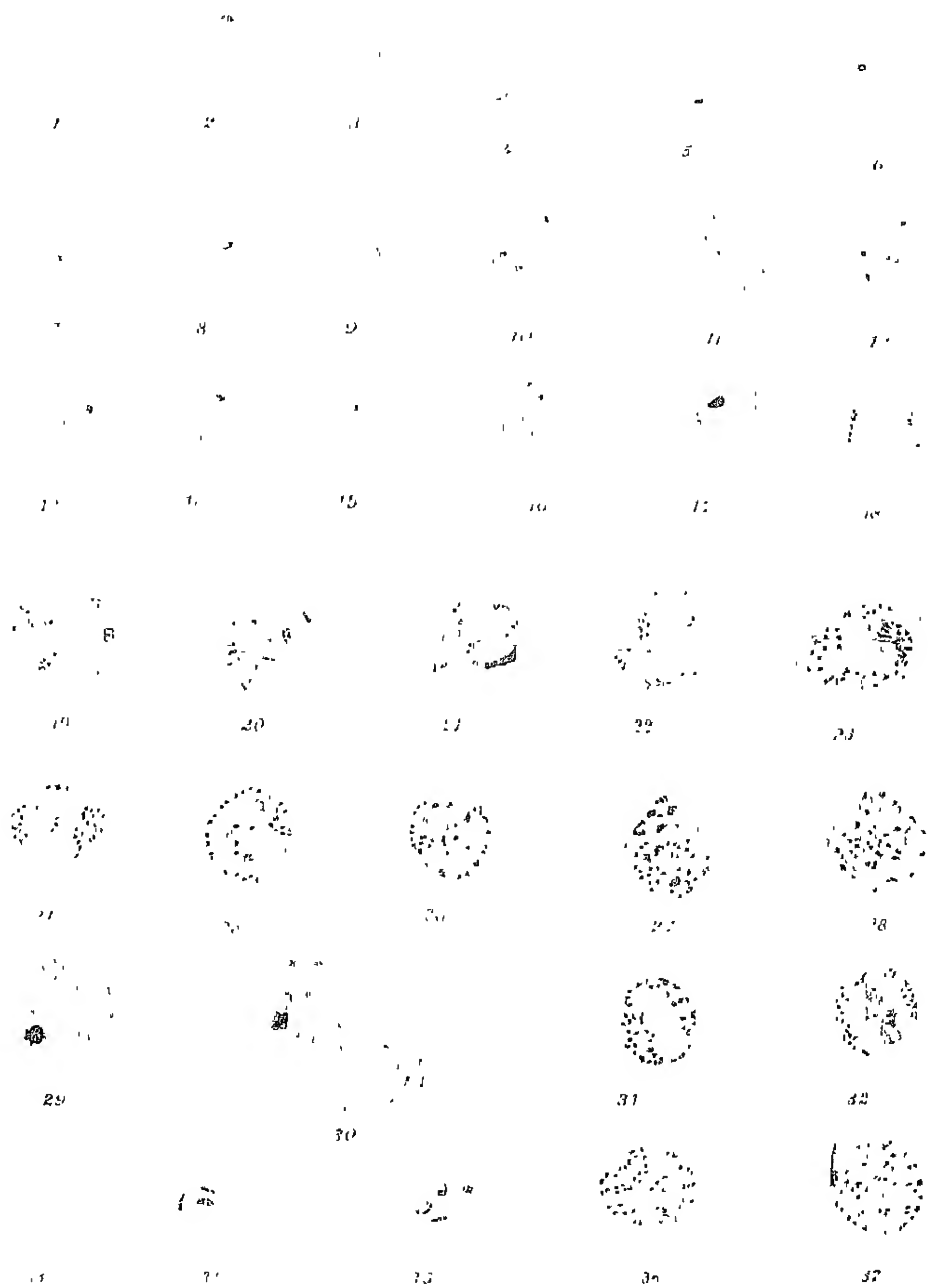


PLATE XII[1]

THE ENDOGENOUS CYCLE OF PLASMODIUM FALCIPARUM

Figs. 76–78. Rod-like *appliqué* or *accolé* forms, attached to the outside of the cell, Fig. 77, double infection, and Fig 78, quadruple infection of a cell.

,, 79–89 Ring forms Figs 79–81, rings attached to the edge of the corpuscle, that of Fig 81 projecting outwards. Figs 84 and 85, the infected cells show Maurer's dots; the latter figure, in addition, shows crenation of the corpuscle, which sometimes occurs Figs. 86 and 87, elongation and commencing division of the nuclear rod, prior to the occurrence of two nuclear granules in the ring (cf Fig. 88) Figs 88 and 89, double and triple infection of the host-cell

,, 90–93. Growing trophozoites (solid-looking forms); that of Fig. 91 is developing attached to the outside of the cell. Note that the pigment is concentrated in a dense mass. The size of the host cell remains practically unaltered

,, 94–99. Stages in schizogony up to the formation of nuclei in the dividing schizont All these stages are from the peripheral blood, but no completely separated or liberated merozoites were found in this situation For later stages see Figs 130 and 132, Pl. XIII

,, 100–107 Young growing gametocytes ("crescents"). The pigment is more or less scattered throughout the parasite. From an early stage the developing crescent has an elongate angular shape. Note the extension of the nucleus, at first in the form of a thick line, along the side of the body Figs. 102 and 106 are probably male forms; 101 and 107, probably female.

,, 108–111. Male crescents Figs. 108 and 109, immature forms; 110 and 111, mature forms. Fig. 109 shows the remains of the cell-substance, in the form of a sheath, around the parasite, note the large vacuole in the host cell

,, 112–117. Female crescents. Figs 112–115, more or less immature forms; Figs. 116 and 117, mature forms. In Figs 114 and 115 the host cell shows the same condition as in Fig 109.

[1] From J. D THOMSON and H. M WOODCOCK's article, "The Parasites of Malaria," in BYAM and ARCHIBALD's *Practice of Medicine in the Tropics*, Vol. II.

PLATE XI.

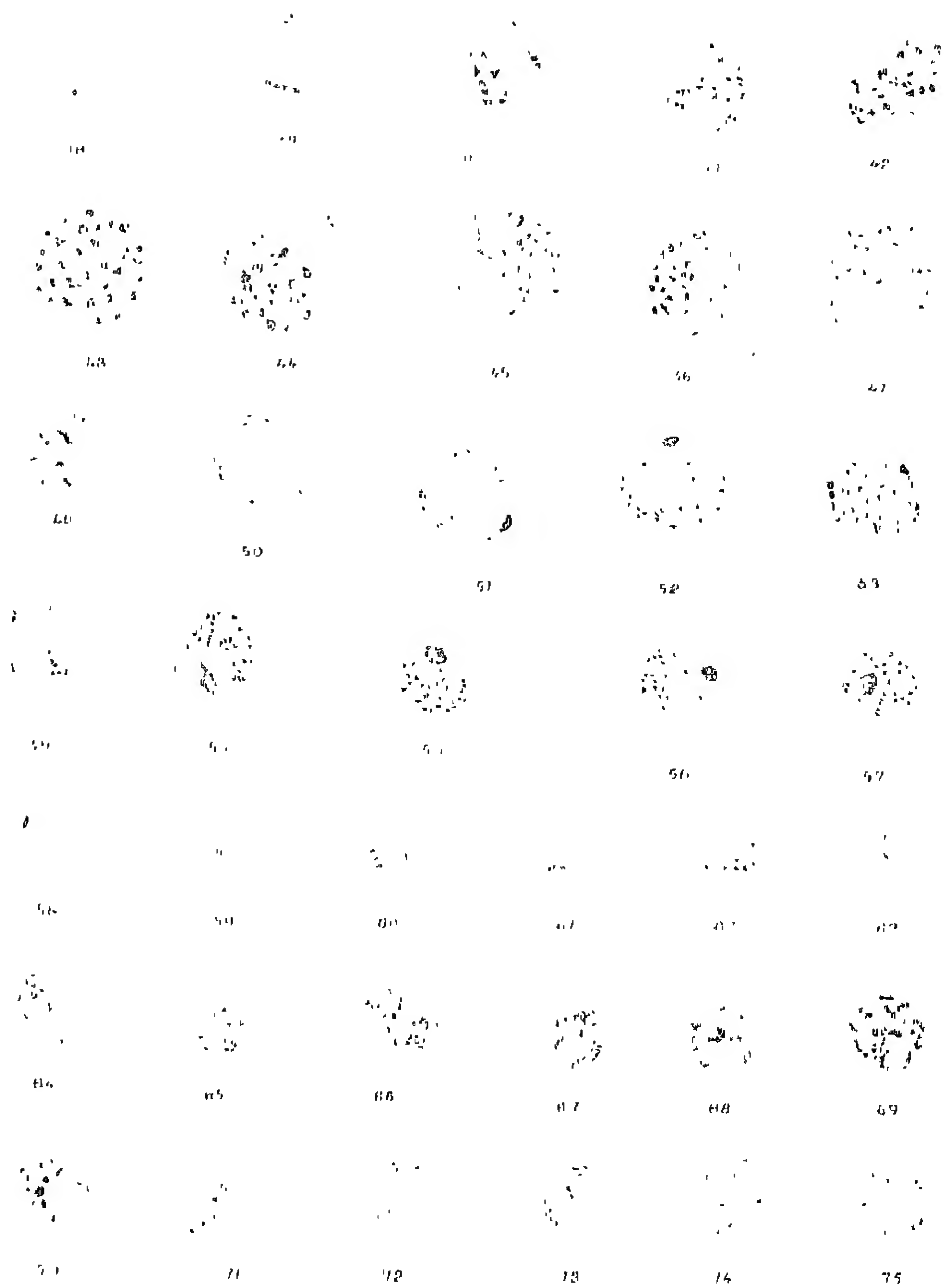


PLATE XIII[1]

THE DEVELOPMENT OF PLASMODIUM FALCIPARUM (continued); SPLEEN AND BRAIN SMEARS AND SECTION OF INTESTINE FROM MALIGNANT TERTIAN MALARIA

Figs 118–122 Maturation and gamete formation ("ex-flagellation") in male crescents Figs 118–120, the gametes have become spherical and the "polar bodies" are lying on, or projecting from, the surface; the nucleus (pronucleus) is large and diffuse Figs. 121 and 122, the male gametes, as thread-like filaments of chromatin, projected from the surface of the parasite. In Fig. 121 they appear to arise from a pinkish body separate from the nucleus; in Fig. 122 they are protruded from a small area directly connected with the nucleus.

,, 123–129. Maturation of female crescents. The limiting membrane here retains its shape, and the gamete escapes from an opening near the middle of the long axis, leaving behind, or carrying with it, the intensely staining "polar bodies." Figs 123–127, stages in the escape of the gamete from its capsule. Fig 128, a gamete completely separated from its capsule, but still carrying a polar body attached to its surface. Fig 129, the nucleus is here smaller and more compact than usual; possibly this represents a zygote?

,, 130. Spleen smear from a fatal case of malignant tertian malaria. The field shows three sporulating parasites and four young, intracellular forms. Note the macrophages, at the lower left-hand side, containing masses of pigment (see p. 232).

,, 131 Brain smear from a fatal case of malignant tertian malaria. The field shows two capillaries containing many parasites, all apparently half-grown, or three-quarter-grown, schizonts (see pp. 234, 235).

,, 132. Section of intestine from a fatal case of malignant tertian malaria The field shows a capillary full of parasites at different stages of development, from nearly full-grown schizonts, to merozoites being liberated (see p. 233).

[1] From J. D. THOMSON and H. M WOODCOCK's article, "The Parasites of Malaria," in BYAM and ARCHIBALD's *Practice of Malaria in the Tropics*, Vol II.

PLATE XII.

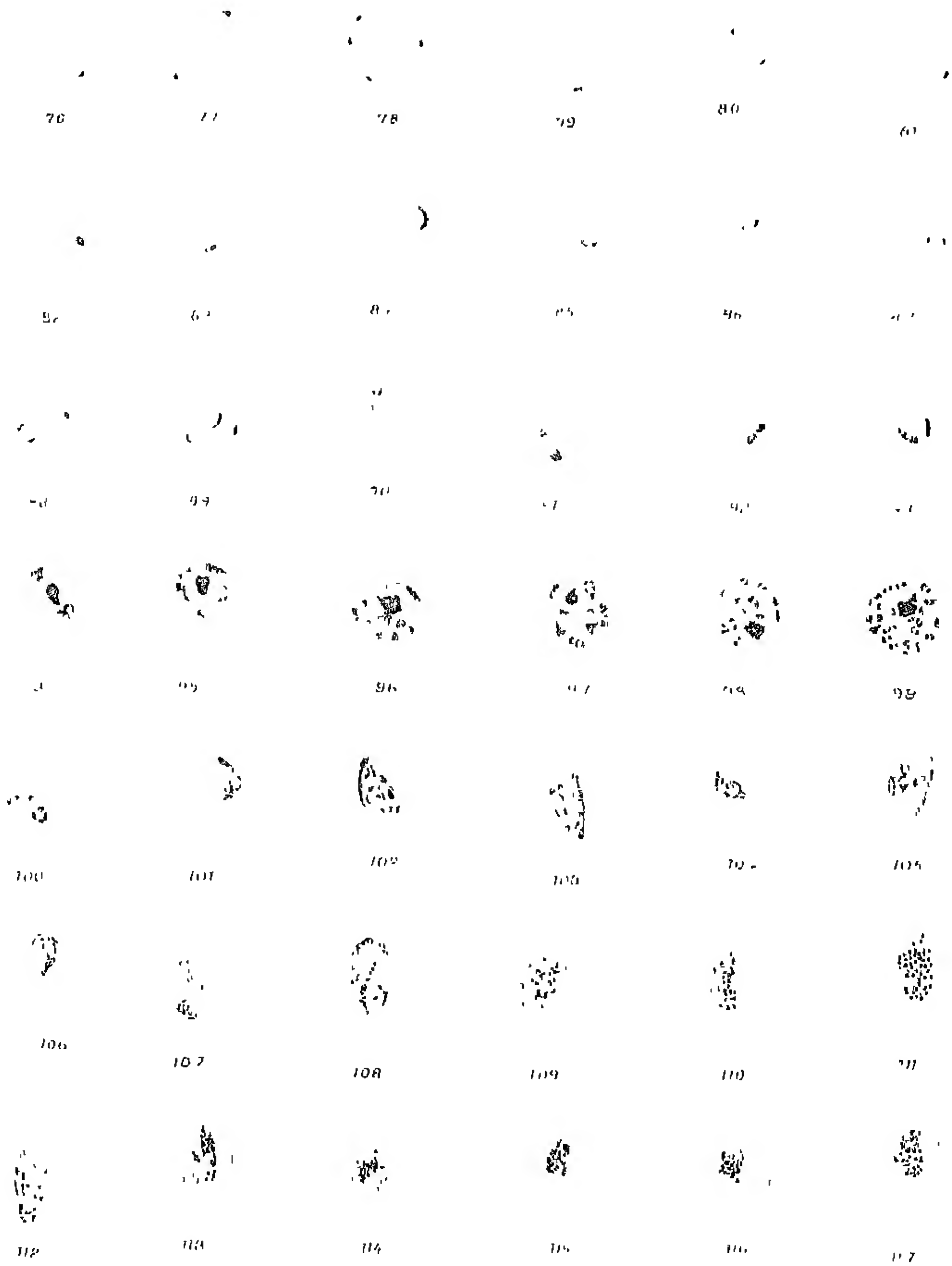
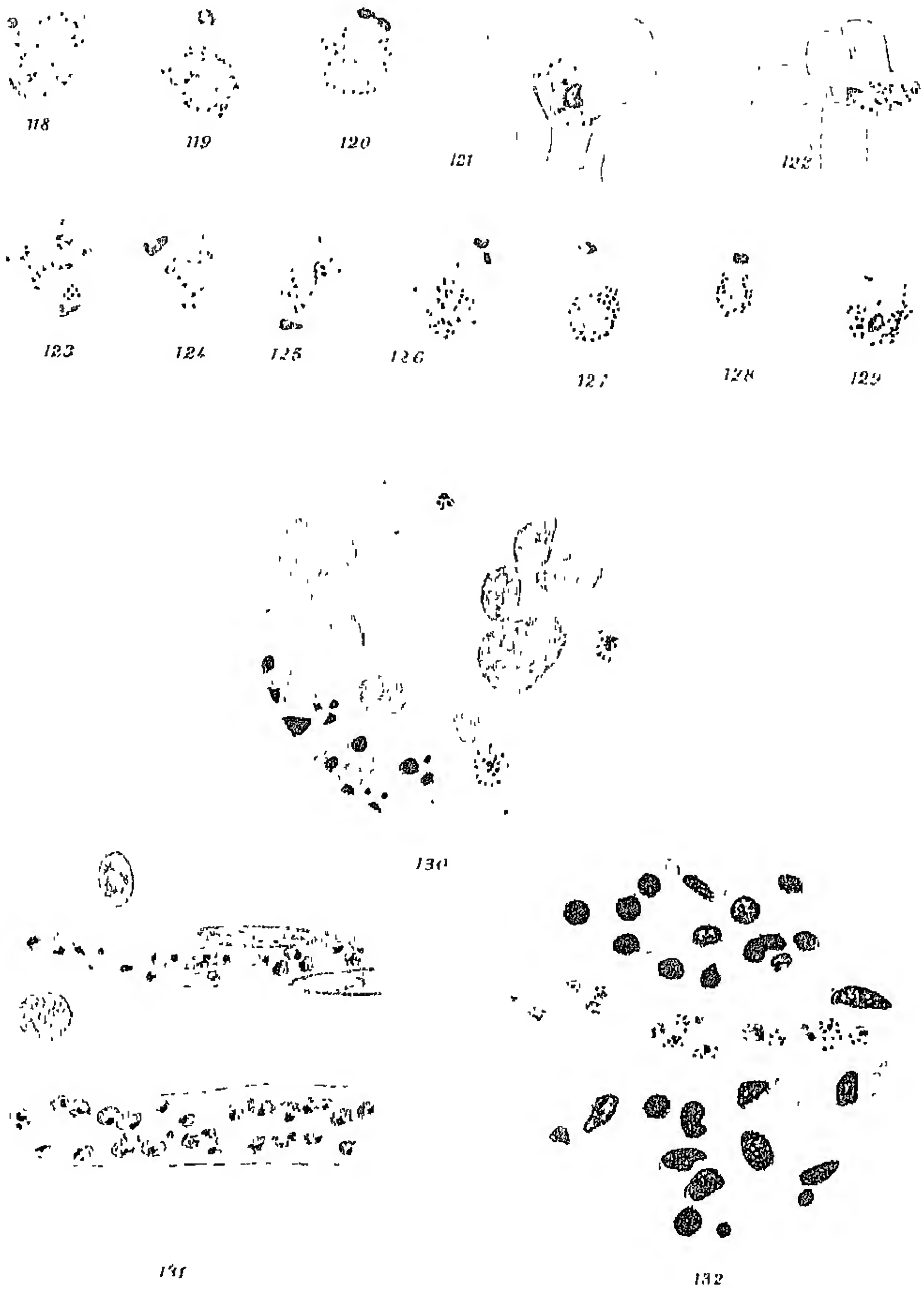


PLATE XIII



the chromatin is diffused. The cytoplasm stains blue and has a loose appearance ; one or two vacuoles may be present. The first stage in schizogony is simple nuclear division, recurring repeatedly by binary division. The resultant nuclei number fifteen to twenty-six, the average being eighteen to twenty. In certain circumstances the schizont may divide before it reaches full size ; then the number of daughter nuclei is fewer. The nuclei are distributed uniformly throughout the body ; the pigment collects in one or two clumps near the middle (Plate X, 28). The cytoplasm segments, a small portion being arranged around each nucleus, and the parasite assumes the mulberry-like character. The merozoites separate from one another (Plate X, 29) and are set free by rupture of the red cell (Plate X, 30), leaving behind the pigment and remains of the cytoplasm. Each merozoite is a little rounded or ovoid body with an average diameter of 1·5 μ. The process of multiplication occupies six to eight hours, the time occupied by the whole schizogonic cycle being forty-eight hours. The free merozoites quickly enter fresh red cells and start the process *de novo*.

In the early paroxysms sporulation occurs, in the vast majority of schizonts, simultaneously. Later on, especially in chronic cases, sporulation is not synchronous, so that there occur in the same brood new small rings within some red cells, while in others the stage of nuclear multiplication is only beginning. When sporulation is more or less synchronous but delayed, the paroxysm *postpones*. Conversely, all the parasites may grow more rapidly than usual, in which case the paroxysm *anticipates*.

***P. vivax* gametocytes.**—They are spherical. The *female gamete* is larger than the red cell ; is rather granular and the dark brown pigment is more abundant than the yellowish brown pigment of the male. Full-grown gametes have the pigment distributed, and the chromatin in a single aggregation—just the opposite of the non-sexual parasite. The *male gamete* stains a light greyish blue, and has a large amount of chromatin, usually centrally placed ; the *female gamete* stains a pure blue, and has only about one-tenth as much chromatin as protoplasm, with the chromatin often placed at one side. In the earliest stage the gametocyte is a small solid-looking body and not ring-shaped. Its growth is much slower—it takes twice as long as a schizont to reach maturity. The cytoplasm has no vacuole. It is decidedly less active and so does not show the great variation in form seen in the growing trophozoite, its shape remaining somewhat rounded or ovoid. When mature the microgametocyte is about the size of a full-grown schizont, the macrogametocyte decidedly larger (from 12 to 14 μ in diameter). The sexes are distinguished by the nucleus of the male (Plate X, 31, 32) being large and diffuse, frequently spreading across the body like a spindle ; in the female (Plate X, 36, 37) the nucleus is small, compact, stains more deeply and is generally situated near the periphery of the body. In the female the cytoplasm is granular and stains intense blue ; in the male it is more hyaline and stains a light greenish blue or pinkish blue tint (Plate X, 31, 32). It is not easy to distinguish a young macrogametocyte and a full-grown schizont that has not commenced nuclear division. Females preponderate. Young ones are rare in the surface blood, as they develop in internal organs.

Malignant Tertian [1] (or Sub-Tertian) Parasite

Malignant tertian (sub-tertian) fever is due to *Plasmodium falciparum* (Plate XII, Figs. 76–117, and Plate XIII, Figs. 118–129), in which the cycle

[1] As the severer types of malarial fever are more frequently associated with *P falciparum*, it is called the *malignant* tertian parasite.

and loses its hæmoglobin. It acquires a characteristic stippled or dotted character. The dots, known as Schüffner's dots, fine at first, become coarse and prominent. In stained films the dots are pinkish, and may be present even during the ring stage (Plate X, 6). "The showing up clearly of this feature depends largely, particularly in cells where the parasites are fairly young, upon the stain used, its strength, and the length of time for which it is used."[1] The infected red cell may be twice its normal size eventually, and is then colourless except for the conspicuous Schüffner's dots. When the dots are absent the remains of the red cell may appear as a mere shadow. The greatly enlarged red cell is frequently caught in the capillaries of the viscera, where sporulation generally takes place. The sporulating forms are therefore not often seen in

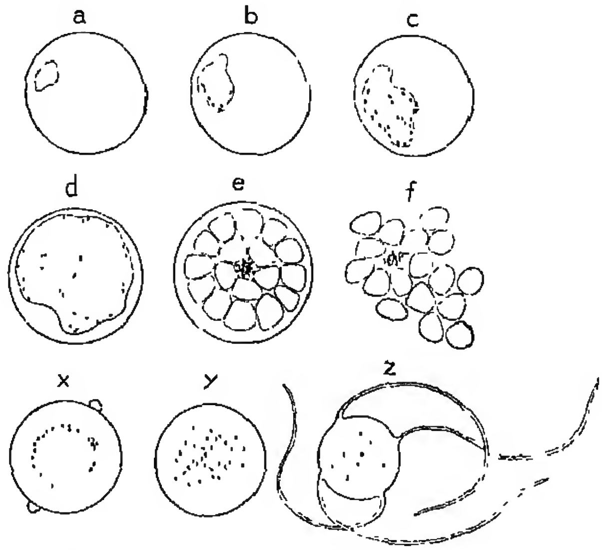


FIG. 58.—*a* to *f*, Phases in asexual development of the benign tertian parasite; *x* to *z*, phases in the sexual development of the same parasite.

From DANIELS and NEWHAM'S *Laboratory Studies in Tropical Diseases*, 5th Ed.

the peripheral blood, but can be recovered from the liver, spleen or other deep-seated organs. The parasites also infect punctate basophilic corpuscles, which are met with, especially in chronic malaria (Plate X, 11).

Pigment in red cells.—As the red cell is absorbed, grains of pigment appear. At first the grains are minute and scanty; the granules increase in size and number with the growth and development of the trophozoite, and, in the later stages of development, are seen as yellowish brown angular particles or rodlets, scattered uniformly in the protoplasm. In unstained specimens the pigment grains are brightly refringent "and doubly refractive when viewed with polarised light."[2] The granules are moved about actively by the currents in the cytoplasm.

Schizogony.—The full-grown schizont is more or less rounded, almost inactive, much larger than a normal red corpuscle, and averages 9 or 10 μ in diameter (Plate X, 22, 23). The nucleus is large and often near the periphery;

[1] J. D. THOMSON and H. M. WOODCOCK, "The Parasites of Malaria," in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. II, p. 1518.
[2] *Ibid.*, p. 1519.

The developing schizont of *P. falciparum* has a distinctly more substantial appearance than that of benign tertian; it is likewise less vacuolated; its amœboid movements cease early, and it then remains throughout as a rounded structure; the hæmozoin occurs in well-formed blocks, and as a rule is in one dark brown conspicuous mass in unstained blood.

Nuclear division begins early. "As the development advances the invaded corpuscles are filtered out by the capillaries and small arteries of the deeper viscera and of the bone-marrow; they are specially numerous in such organs as the spleen and the liver."

Plate IX, Fig. 3, shows *Plasmodium falciparum* in fresh unstained blood. *a*, *b*, *c*, Early stage. Comparatively much smaller than either quartan or benign tertian. In the earlier unpigmented phase, owing to minuteness and its forming a very transparent object in the hæmoglobin, it is hard to see. *d*, Indicates the very active movement seen when the fresh blood is examined at once. In a short time the amœboid activity declines, and then the young parasite becomes more passive and forms a definite, easily seen, rather bright, colourless ring, *a*, *b*, *c*, *e*. Sometimes the ring reverts time after time to the amœboid condition, but ultimately remains as a ring. *g*, Two rings in one red cell. *i*, *j*, Segmenting form of the malignant tertian parasite, seldom seen in the peripheral blood. *e*, "Brassy body" of the Italian malariologists. *k*, Male crescent. *l*, *m*, *n*, Changes in male crescent before flagellation. *o*, Flagellated male crescent.

In artificial cultures the growing parasites of the sub-tertian form show a tendency to clump; this is not seen in the same circumstance in benign tertian.

Growing forms of *P. falciparum* are seldom found in the surface blood but in heavy infections half-developed schizonts and an odd rosette occasionally appear. Conversely, in rare instances schizogony takes place actively in the peripheral circulation.

The size of the infected red cell is not altered; in the later stages of development the cell is paler. Instead of Schuffner's dots we have Maurer's [1] clefts (Plate XII, 84, 85), which are decidedly larger, more irregular, and fewer in number than Schuffner's dots in benign tertian malaria, and stain a deeper or darker red and not pink. They are very characteristic, but are much less frequently met with in malignant tertian than Schüffner's dots are in benign tertian. They are large, irregular and coarse-looking from the beginning and do not alter; they give the infected red cell a blotchy character. Schuffner's dots are very delicate and small at first, becoming more conspicuous as the changes in the red cell progress. Young forms of schizonts of malignant tertian and benign tertian may be in the peripheral blood at the same time. What generally attracts attention to the mixed infection is the detection in the same slide of crescents and developing schizonts of benign tertian malaria. Rarely the two forms of parasite may occupy the same cell. In fresh-blood specimens red cells infected with *P. falciparum* are occasionally met which are somewhat darker than normal and have the colour of old brass—"brassy bodies."

The pigment in the growing schizont is well developed and compact.

The fully formed schizont is the smallest of the asexual schizonts, being only from 1·5 to 5 μ in diameter; much of the red cell is not occupied by it. The division of the nucleus occurs rapidly (Plate XII, 94–98). The average number of merozoites found is from 14–16, but they may vary from 6 to 32, and in the same case the number of merozoites varies very much. These average

[1] STEPHENS and CHRISTOPHERS have priority over MAURER as regards the recognition of these clefts or dots.

of development occupies forty-eight hours, but sporulation does not ordinarily occur simultaneously. The fully developed intra-corpuscular form is not seen in the blood removed from the finger for examination. The gametes are peculiar in having a crescentic shape, and hence are called "crescents."

The early unstained, unpigmented stage is difficult to see (Plate IX, 1, *a*). Amœboid movements are active at first; later the parasite forms small colourless rings, slightly smaller than in other types, 1·25 to 1·50 μ in diameter (Plate XII, 79–82), though occasionally rings as large as those of benign tertian are found (Plate XII, 83, 84). The youngest stained malignant tertian parasites are very small, well-defined blue signet rings, often elongated, with a bright red chromatin dot at one end and a clear area between it and the cytoplasm; the medium-sized parasites are large rings with less regularity; the larger forms are irregular blue structures with a bright mass of chromatin. "All stages in the elongation of the nuclear rod and its separation into two parts can be found (Plate XII, 84–87). This fragmentation of the nucleus is more common in malignant than in benign tertian rings."[1] *Plasmodium falciparum* rings frequently project partially from the red cell, the inner part of the ring causing the margin of the corpuscle to be indented (Plate XII, 81). Unless the slide is well made these forms may be missed. Such marginal rings and young schizonts are frequently met with—the *accolé* and *appliqué* forms (Plate XII, 76–78). "Frequently the parasite appears only as a short, narrow blue streak of cytoplasm with a red nuclear dot."[2] Double and multiple infection of the red cell is more frequently met with in malignant tertian than in other types of infection; especially in fresh infections. In really heavy infections such as occur in epidemic malarial seasons in India multiple invasion of red cells is very common (Plate XII, 78, 89). Occasionally in heavy infections all sorts of strange developmental forms are met in the peripheral blood. Schizogony occurs chiefly in the internal organs—sinuses of spleen, bone-marrow, brain, and in the capillaries, etc.

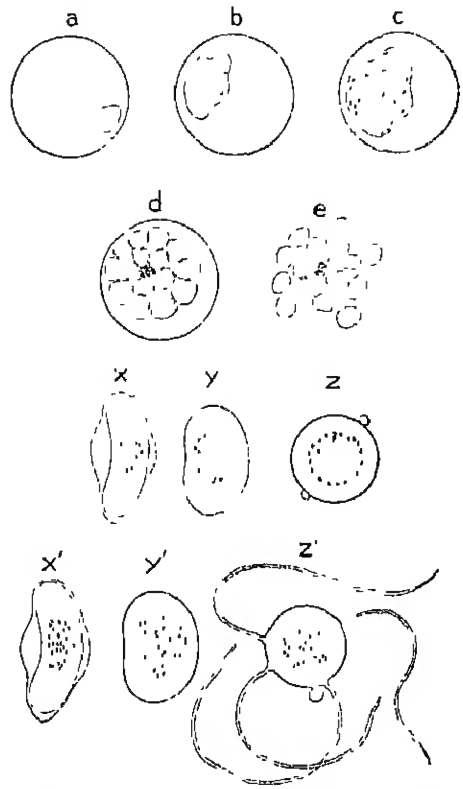


FIG. 59.—*a* to *c*, Phases in the asexual development of the malignant tertian parasite; *x* to *z*, phases in the sexual development—*x y z* of the female, *x′ y′ z′* of the male.

From DANIELS and NEWHAM'S *Laboratory Studies in Tropical Medicine*, 5th Ed.

[1] J. D. THOMSON and H. M. WOODCOCK in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. II, p. 1530.

[2] *Ibid.*

smaller, and is seen as a more or less central mass; the protoplasm is granular; the pigment grains are likewise collected together at or near the centre in close relation with the nucleus, which they often partly hide. The pigment granules in both sexes remain individually separate. A fully formed crescent has in its development used up the whole substance of the red cell it occupied: the outline of the remains of the red cell is seen, often very dimly, in the concavity of the crescent, but *never* extends from one pole to the other. In immature crescents the red cell is partly occupied and can often be seen to form a narrow covering around the parasite (Plate XII, 109, 112–115), more distinctly visible at the concavity. When over-stained this sheath-like covering is seen as a well-marked red zone around the parasite.

The developing forms of the crescent are seldom met with in the peripheral blood. "When found they have been mistaken for cystic or other stages of the cycle held by some to be responsible for certain aspects of relapse or the continuation of the life of the parasite during and after quinine treatment." [1] These may be the "resting forms" described by several authors. The writer believes that practically nothing is known regarding the development of crescents. Young gametocytes (Plate XII, 101–107) are distinguished from growing schizonts by the somewhat elongate angular shape, and by the pigment not showing any tendency to form a solid mass. They are to be found in the spleen and bone-marrow about the fourth day of the sub-tertian attack; crescents are not often found in the peripheral blood until they are mature, which is about the tenth or eleventh day from the beginning of fever. In some cases of malignant tertian malaria crescents do not develop for a fortnight, three weeks or even longer after the first paroxysm. Why this is so we do not know. The nucleus is small and at one or other end. "A peculiarity which we have noticed is that the nucleus, at this stage, appears to be drawn out, in the form of a coarse line (Plate XII, 101), staining the same red colour, running along the periphery of the body. We have seen this appearance both in what we regard as male (Plate XII, 105) and female (Plate XII, 107) young gametocytes. Subsequently the nucleus passes to the centre and takes up its usual position." [2] Plate XIII shows the maturation and gamete formation in male (Figs. 118–122) and female (Figs. 123–129) crescents.

In fresh infections crescents are rare. The blood may be surcharged with parasites before crescents appear. In old infections and chronic malaria we may get large numbers of crescents when no rings at all are visible. Crescents may be consistently absent in adults and present in their infected children.

Effete crescents show vacuolations in the protoplasm indicative of degeneration. According to J. D. THOMSON, individual crescents do not live in the peripheral circulation for more than two days. He states that male and female crescents possess a definite true membrane or envelope, which does not appear to be demonstrable by staining, so long as the crescents remain unaltered in the blood, but it is easily seen when their further development is initiated, *i.e.* artificially.

The malignant tertian parasite, during its sexual cycle in the female Anopheles, is said to be more susceptible to the influence of cold than the tertian and quartan types; hence it is not so widely distributed geographically as the benign types and occurs mainly in the warmer parts of the tropics and sub-tropics.

[1] W. M. JAMES, *International Conference on Health Problems in Tropical America*, 1924, p. 69.

[2] J. D. THOMSON and H. M. WOODCOCK in BYAM and ARCHIBALD's *Practice of Medicine in the Tropics*, Vol II, p. 1534.

0·71 to 1 μ in diameter, and are therefore decidedly smaller than those of *P. vivax*. There is less uniformity as regards time taken in the development of the malignant tertian parasite than in the other types—the pace at which schizogony progresses is much less uniform than in the simpler infections. In India schizogony takes from thirty to forty hours, but there is often a want of synchronism in the full development of the schizonts. Whilst the majority may sporulate within a few hours of one another the remainder continue to sporulate for many hours, even for a whole day. Rings, the result of infection of red cells from recent schizogony, can be found in the surface blood during the whole period of a paroxysm; they may be few or many, showing that sporulation is continuous throughout the time. This explains the remittent (or continuous) and sometimes irregular type of the pyrexia in this infection.

BLACKLOCK, in a report on a case of malignant tertian infection ending fatally, suggested that the optimum habitat for the segmenting forms is the spleen and that for crescents is the bone-marrow. DARLING considers the bone-marrow of ribs the main focus for crescents.

J. D. THOMSON and H. M. WOODCOCK [1] summarise the difference between malignant tertian and benign tertian rings as follows

"1. If the marginal forms (*i.e.* appliqué forms or projecting rings) are found in any number, a malignant tertian infection is certainly present.

"2. If, as sometimes is the case, few of these forms occur, the more uniform appearance of the rings, the frequent occurrence of parasites with two nuclear granules, and a fair proportion (relatively to the degree of infection) of doubly infected cells taken together, are very suggestive of malignant tertian.

"3. In a benign tertian infection, especially if at all heavy, a few rings will usually be found, irregular in appearance or slightly in advance of the others as regards growth, and beginning to send out pseudopodial processes. Indications of enlargement of the cell and a slight alteration in colour may also be noted here and there."

Should any doubt exist, the examination of another film taken some hours later will settle it. We should constantly bear in mind the possibility of a mixed infection of both types of tertian.

"It is curious that just before the paroxysm begins the number of parasites in the peripheral blood may be comparatively few, yet phagocytes containing blocks of pigment are usually fairly abundant. In cases in which malignant tertian malaria is suspected, and where parasites are absent in fresh blood, we should never omit the examination of dried specimens of the blood by the Romanowsky method, in which the blue rings, with deeply stained chromatin dots, are more rapidly 'spotted' than the delicate hyaline bodies in fresh blood" (THAYER).[2]

Malignant tertian gametocytes—crescents.—Characteristic crescents are fairly large and distinctive bodies, very obvious in both fresh and stained preparations. Most of the mature crescents are really sausage-shaped with rounded ends (Plate XII, 110, 116). They vary from 9 to 14 μ long and 2 to 3 μ broad. The *male crescent* (Plate XII, 110, 111) is the broader; its nucleus is extensive and may be diffused over the greater part of its substance; its pigment grains are scattered and may extend to near the poles. In a well-stained crescent film the males can be picked out at once by their *red* colour—the whole crescent seems to be red and the difference from the female is very marked. In the *female crescent* the nucleus is much

[1] BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. II, p. 1531.

[2] ALLBUTT and ROLLESTON'S *System of Medicine*, Vol. II, Part II.

PLATE XIV

MALARIA PARASITES. $\times$ 2,000

A. SUB TERTIAN PARASITE (*Plasmodium falciparum*)

Fig. 1 Sub-tertian rings, heavy infection. Note the marginal form, and in some the double chromatin dots.

" 2. Parasites twelve hours old, approximately, from a brain smear At this stage they become arrested in the capillaries. Note early and characteristic concentration of pigment.

" 3. Parasite, twenty-four hours old, from an artificial culture, forms seen usually in the capillaries of internal organs

" 4. Complete schizogony, with separation of merozoites, from spleen smear

" 5. Complete schizogony, from brain smear of a fatal case.

" 6. Male gametocyte (crescent), with remains of red cell, from peripheral blood.

" 7. Female gametocyte (crescent), staining a darker hue, with concentration of chromatin and pigment

" 8. Exflagellation of male gametocyte

B. BENIGN TERTIAN PARASITE (*Plasmodium vivax*)

Fig. 1 Young ring form in peripheral blood.

" 2. Amœboid forms. Note the Schuffner's dots and a slight enlargement of corpuscle.

" 3. Amœboid form, a quarter grown. Note formation of pigment in cytoplasm, Schüffner's dots, and increased size of corpuscle.

" 4 Schizont, showing early division of chromatin.

" 5. Complete schizogony in peripheral blood, with formation of twenty merozoites.

" 6. Male gametocyte. Note loose arrangement of chromatin, pale cytoplasm, and smaller size than female.

" 7 Female gametocyte Note compactness of chromatin, and darker-staining cytoplasm.

" 8. Double infection of single corpuscle with gametocyte and schizont

C. QUARTAN PARASITE (*Plasmodium malariæ*)

Fig. 1 Young ring form.

" 2. Partially grown form, compact parasite with coarse pigment

" 3. A more fully grown stage than Fig. 2.

" 4. Early division of chromatin in young schizont.

" 5. More fully grown schizont, with chromatin divided into eight masses. Note coarse and scattered pigment.

" 6. Complete schizogony, showing typical rosette with centrally placed pigment and formation of eight merozoites.

" 7. Characteristic " band form " of young quartan parasite

" 8. Male gametocyte

" 9. Female gametocyte, with coarser pigment and darker-staining cytoplasm.

Table of Differences between the Three Species of Malaria Parasites

—	*P. vivax.* Tertian	*P. malariæ* Quartan.	*P. falciparum* Sub-tertian
(1) Length of cycle, *i.e.* interval between one sporulation and the next	48 hours	72 hours	Uncertain, often about 48 hours or rather less
(2) Size of mature parasite	Larger than the average red corpuscle	Slightly smaller than the average red corpuscle	Distinctly smaller than a red corpuscle
(3) Number of "spores"	14–24, average 18–20	6–12, average 8 or 9	Variable 6–32; average 20–24
(4) Amœboid movement	Active and extensive	Sluggish in immature forms	Very active, but range of movement not extensive
(5) Gametocytes	Rounded bodies or slightly ovoid; larger than the red cell	Rounded or slightly ovoid; about same size as red cell	Sausage-shaped or crescentic—*crescents*
(6) Pigment	Finely divided and yellowish brown	Coarse and dark brown	Black and at first finely divided, but soon aggregates into coarse granules
(7) Effects on red corpuscles serving as host	Causes it to swell and become paler. In stained specimens Schüffner's dots often found	Red corpuscle not enlarged; may become slightly smaller and darker; no stippling	The young parasite causes little or no alteration but sometimes the corpuscles become yellower—"brassy bodies." Sometimes contains coarse dots or irregular mottling (Maurer's dots or clefts)
(8) Trophozoites	Signet rings of various sizes; growing forms irregular in size with vacuolation	Signet rings as in *P. vivax*; growing forms angular or band like; vacuole soon disappears	Rings small, often containing two nuclear granules, and sometimes attached to edges of red cell
(9) Relative number of parasites in peripheral and visceral blood	Parasites numerous in all parts of the body in various stages of their cycle	As in *P. vivax*	The greater part of the development of the parasite takes place in the internal organs; hence the relative scarcity of all except most immature forms in peripheral blood
(10) Liability to relapse	Relapses noted up to 3½ years from time of original infection	Infection persistent. Relapses may occur for 6 years or more from time of original infection	Much less than in other two forms; infection intense in early stages. Relapses seldom occur after 9 months from time of original infection, maximum period observed, a few years

Prof. J. W. W. STEPHENS[1] has described and pictured another Indian species under the name *P. tenue*, which is considered by some malariologists to be probably an exceptional form of *P. falciparum*. Sinton (1922) reported infection with *P. falciparum* in which a "*tenue*" stage occurred during six only of the forty-eight hours of the life-cycle. He used the ordinary

[1] *Annals of Tropical Medicine and Parasitology*, Vol VIII (1914), p 119.

Ross has shown that blood must come into contact with air for ex-flagellation to take place in male crescents, for if air is excluded in making a fresh preparation it does not occur. Adding a little moisture hastens ex-flagellation; both air and moisture are added by breathing on the droplet of blood before adjusting the cover-slip. Males ex-flagellate only when mature.

It is curious that some mature male crescents free from any visible degenerative changes do not ex-flagellate, no matter how we attempt to make them do so; the writer is not aware that the cause of this failure has been explained. In some of these failures the patients have been taking large doses of quinine; but the failure also occurs sometimes in those who have never taken quinine.

Crescents are very common in chronic infections, and in these cases they may sometimes be found for weeks on end without any asexual forms being seen in the blood, when examined as ordinary smears; in such cases a thick-film preparation will sometimes reveal the presence of rings, though they may be few.

P. falciparum develops more sexual forms than the other species. *P. vivax* gives rise to more frequent relapses with the appearance of sexual forms in the surface blood; therefore there are more numerous opportunities for infecting anophelines. *P. malariæ* produces fewest gametoctyes, but these are said to continue in the blood longest.

Plate XIV shows the asexual and sexual forms of the three malaria parasites, stained with Leishman and highly magnified.

The view once favoured by some distinguished malariologists was that the sexual forms of malignant tertian were formed by the union (syzygy) of two rings in one red cell. JULIUS MANNABERG,[1] in *The Malaria Parasites*, Plate IV, Figs. 27–32, shows the stages by which this union is supposed to be effected. The explanation seems to be that, in sub-tertian blood, of two rings in one red cell one grows up and produces a schizont, while the other develops into a crescent, both maturing within the cell. The same may sometimes be seen in benign tertian. Plate XI, Figs. 43–49 show different combinations of two parasites growing and maturing in the same red cell. Figs. 43–47 relate to *P. vivax*, 48 and 49 to *P. falciparum*. See also Fig. 71, p. 218. J. W. W. STEPHENS considers that parasites divide into two in the peripheral blood; this is a rare incident, but the evidence of its occurrence is quite clear in the films described. The writer believes that he met with such division as long ago as 1901. Twin crescents are very occasionally met with in sub-tertian surface blood (Fig. 60).

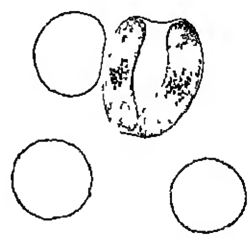


FIG. 60.—Twin crescent. From MANSON'S *Tropical Diseases*, 8th Ed.

The Table on p. 172 gives the essential differences between the three forms of malaria parasites met with in India.

Question as to the existence of a quotidian malignant malaria parasite in India.—In the literature of malaria in India there is only one reference to a short-cycle form of malignant malaria parasite, and this has not been confirmed The writer has written to various experts on malaria in India to ascertain their experience on the subject, and all except two state that they have not found such a parasite. There may possibly be several other species of malaria parasites in India that we are unacquainted with. It is necessary that we should, by systematic examination of a large number of the cases now diagnosed as double malignant tertian (quotidian), put this out of doubt. This can be done by working out the cycle of the parasites found in such cases.

[1] New Sydenham Society's Translation, 1894.

many as 32. The pigment of *P. falciparum* clumps much earlier in the developing schizont than in *P. vivax*, and is much coarser and more discrete.

The asexual development of all three types of the parasite has been carried out in culture tubes. In the case of *P. falciparum* four successive generations have been grown, and it would appear that with optimum conditions, especially the addition of fresh serum and red cells to the medium as required, the growth and multiplication might go on indefinitely. The development of asexual forms *in vitro* is practically the same in all respects as in the natural state. On one occasion, in a culture tube overlooked for ten days in an incubator, SINTON found many crescents, though none had been found in the original blood.

Regarding the number of merozoites in the mature schizont, it is interesting to state in passing that the merozoites of 100 fully developed segmented *malignant tertian* rosettes, occurring in smears during autopsies by W. M. JAMES in Panama, were counted by R. ROSS and J. D. THOMSON; 13 per cent. contained 32 merozoites and the average for the 100 rosettes was 27—a higher number than is generally given.

Major J. A. SINTON, V.C., I.M.S.,[1] has devised and used a simplified method of artificial culture of malaria parasites. His entire apparatus, with the exception of some glass beads and a pipette, consists of a single piece of glass tubing about a foot long and 4 to 5 mm. in diameter. The original paper should be consulted for details. The best development takes place on the surface layer of red cells, which must be covered by serum at least 12 mm. (preferably 24–48 mm.) deep. "In view of the difficulty of obtaining from the finger of an anæmic malarial case sufficient blood before clotting occurs to produce the requisite quantity of serum, this last is replaced by ascitic fluid or hydrocele fluid. Growth is best at 37° C.; between 38° and 41° development seldom advanced beyond half or two-thirds growth, sporulation being exceptional. In a thermos flask filled with water at 40° C., into which the culture tube was placed, the temperature drops to 38° before it is closed, and thereafter half a degree hourly. A temperature of from 32° to 38° C. is suitable, so that filling such a flask with water at 40° C. every twelve hours produces conditions satisfactory for the growth of sub-tertian parasites."

It has recently been stated by G. L. PEREKREPOW that blood removed immediately before a paroxysm does not culture; blood taken during the onset may grow to two generations; rather later in the attack it gives better results, and after an attack the results were most satisfactory. The failure of the blood removed early is considered to be due to anti-bodies in the serum. The evidence offered is that, substituting for the patient's serum that of one who had never had malaria, culturing was good, and it was nearly as good if the man's own serum, heated previously to 55 or 56° C., were substituted for his untreated serum.[2]

To follow the life-cycle of malaria parasites.—To determine the cycle of a malaria parasite it is necessary:

"(1) To estimate the size and percentage of parasites of each size at any particular time, *e.g.* starting with the onset of the attack.

"(2) To follow each group to its period of maximum development in the circulation.

"(3) To estimate the time between this period and the next appearance of young forms.

"(4) To estimate the time between the appearance of an outburst of young forms and a second similar outburst

"The interval between (1) and (4) should be equal to the intervals of periods (2) and (3). It is more accurate to use a micrometer scale for measuring; but the estimation can be made with considerable accuracy without."[3] To establish a parasite cycle, repeated observations at definite intervals are necessary; the temperature should also be carefully recorded every two hours in working out a possible quotidian malignant, and every four hours in benign tertian, quartan and ordinary malignant tertian; if this repeated examination at short intervals is not carried out, noteworthy changes may be lost sight of

[1] "A Simplified Method for the Cultivation of *Plasmodium falciparum in vitro*," *Ind. Jl Med. Res.*, 1922, pp 203–9.

[2] "Lytic Action of Blood Serum of Patients on Malarial Parasites," *Rev. Microbiol et Epidemiol.*, 1924, Vol. III, No 3. Abstract in *Trop. Dis. Bull*, October, 1922, p 821.

[3] STEPHENS and CHRISTOPHERS's *Practical Study of Malaria*, 3rd Ed., pp 235, 236.

dried films. The locality was Nagpur (C.P.), whence STEPHENS obtained the original specimens from Lt.-Col. W. H. KENRICK, I.M.S.; the symptoms were slight, but the infection heavy. Major H. E. SHORTT, I.M.S., met two cases of malaria with the same form in Shillong (4,500 feet), Assam. (See Appendix VI—5.)

Unity or plurality of species of malaria parasites.—In the last few years several authorities on tropical diseases have resuscitated this question, which was threshed out with such warmth a generation ago. GRASSI, PLEHN, CREMONESE and others have once more advanced the view that there is but one species, which changes its morphology, *e.g. P. falciparum* altering to *P. vivax* with change of season. GRASSI believes that the one species of parasite reappears regularly in the same form at each relapse, except that in March and April (in Italy) the malignant tertian form relapses as benign tertian, and that in prolonged infection the form is likely to change. The evidence put forward now is no more convincing than it was thirty years ago. On the contrary, the arguments against it seem to be incontrovertible. Of the many experimental transmissions of malaria by infected Anopheles that have been carried out, in every case the organism found in the person bitten is the same as that in the original patient. Of the large number of general paralytics who have been inoculated with the benign tertian parasite both by Anopheles and by direct injection of infected human blood, the patients have suffered from benign tertian paroxysms only, and only benign tertian parasites were found in their blood. In some series of cases this inoculation has gone on uninterruptedly with the same strain of *P. vivax* for forty consecutive inoculations, covering all seasons for several years. Comparisons between the types of infection, temperature charts and clinical signs in patients infected early and those infected after several passages indicate that the strain has undergone no increase in virulence during its direct passage through forty-one generations; nor does the morphology of the parasite appear to undergo any change after many passages.[1]

ACTON considers that the various forms of malaria differ not only in the morphology of the parasites, but also in cultural characteristics, incubation periods, symptomatology and reactions to quinine.

The concurrence of two (sometimes three) species of parasites in mixed infections should be sufficient evidence against unity. We are constantly seeing the asexual parasites of both malignant tertian and benign tertian malaria, and with these, occasionally, both species of gametocytes, *on the same slide*. The writer on one occasion saw *in one field* of a stained thin film crescents, malignant rings and developing schizonts of benign tertian.

V.—CULTIVATION OF MALARIA PARASITES

C. C. BASS (1910) was the first to cultivate malaria parasites. His method has been modified and simplified by J. G. and D. THOMSON as follows[2]:

Draw 10 c.c. of malarial blood into a test tube containing glucose solution. Defibrinate by stirring with a thick wire for about five minutes and remove the wire with clot adhering to it. Pour this defibrinated blood into several small sterile test tubes, which should contain at least a 1-inch column. Rubber caps are adjusted, and the tubes are placed in an incubator.

They note the tendency of *P. falciparum* to agglutinate which is not the case with *P. vivax*, and think this agglutination the cause of the plugging of the capillaries in pernicious malaria. They observe that 32 merozoites is the maximum number in sporulation of malignant tertian, while *P. vivax* has only 16 or more, but never as

[1] W. YORKE and MACFIE, *The Lancet*, May 17, 1924, p. 1017 *et seq.*
[2] BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. II, p. 1542

PART II

CLINICAL AND PATHOLOGICAL EFFECTS OF MALARIA IN INDIA

tion. When there is a moderate number of parasites to the cubic millimetre of blood in the later days of the incubation period the victim begins to suffer from a feeling of malaise, lassitude, loss of appetite, headache, vague muscular pains and chilly sensations. With each sporulation the symptoms are aggravated until a definite paroxysm begins with rigors. In the primary malarias induced by the inoculation of infected blood for the cure of general paralysis the incubation period in benign tertian has extended to thirty-one days, in quartan to fifty days, and in sub-tertian to fourteen days.

The Malarial Paroxysm [1]

The term *paroxysm* is applied to the febrile period, occupied by three stages—cold, hot and sweating. The term *interval* is used to denote the period from the commencement of one paroxysm to the commencement of the next paroxysm. The term *intermission* is applied to the period intervening between the end of one paroxysm and the beginning of the next. *Quotidian* is the term applied to malarial paroxysms coming on every twenty-four hours, *tertian* every forty-eight hours and *quartan* every seventy-two hours. When individual paroxysms are prolonged so that one attack is not concluded before the next begins the attack is said to be *subintrant*. When the paroxysm is prolonged and periodicity is marked only by a slight fall of temperature and slight sweating the fever is called *remittent*; when there is no remission the fever is said to be *continued*. When the temperature goes regularly to fever height and then drops to below normal it is *intermittent*.

When the parasites have increased in numbers sufficiently to produce enough malarial toxins to give rise to fever, the typical manifestation of malarial infection, *the malarial paroxysm*, begins. At this time all the red cells that are infected burst more or less simultaneously, and set free many millions of spores and a corresponding amount of toxins and melanin.

Premonitory symptoms.—As the parasites are multiplying and approaching a number sufficient to give rise to an attack of fever, certain premonitory symptoms develop, such as general malaise, lassitude, yawning, aching in the limbs and back, headache, chilly sensations, and slight rises of temperature daily, loss of appetite, and nausea, before the fully developed attack. These symptoms may continue some days before the paroxysm sets in. Occasionally there are no premonitory symptoms, the cold stage setting in abruptly.

Symptoms.—The paroxysm in all forms of malarial fever consists, as stated, of three stages—*cold, hot* and *sweating*, which may be more or less modified according to the species of the parasite, peculiarities of the individual, degree of susceptibility or sensitiveness to the effects of the malarial toxins, etc. The attacks commence about the same hour, simple and malignant tertian attacks usually about midday, and quartan in the afternoon; in mixed infections with quotidian attacks the cold stage begins between 9 and 11; there are many exceptions to these rules. Sometimes, however, attacks change their rhythm and begin sooner or later than usual. If a paroxysm which has been coming on at 11 a.m. begins at 9 or 10 a.m. it is said to *anticipate*; when it commences at 1 or 2 p.m. it is said to *postpone*. Septic fevers usually begin late in the afternoon or in the evening.

Cold stage.—There are peculiar chilly sensations, fleeting pains in various parts of the body which come and go but increase in severity; then the chilliness increases rapidly, the patient begins to shiver and is as a rule compelled to go to bed. A regular shivering fit now usually occurs. Tremors of the muscles

[1] From the Author's *Hygiene and Diseases of India*, 3rd Ed., p. 751 *et seq.*

PART II

CLINICAL AND PATHOLOGICAL EFFECTS OF MALARIA IN INDIA

A.—MALARIAL FEVERS OF INDIA

SYNS.—*Eng.*—Malaria, Malarial Fever, Paludism, Marsh Fever, Jungle Fever, Periodic Fever, Paroxysmal Fever, Ague, Fever and Ague, Intermittent Fever, Remittent Fever, Malarial Remittent Fever, Sub-tertian Fever, Tertian Fever, Quartan Fever, Æstivo-Autumnal Fever, Chill Fever, Pernicious Fever, Coast Fever, Fever of the Country. There are likewise various local names given to malarial fevers in India, such as Terai Fever, Peshawur Fever, Assam Fever, etc. *Fr.*—Paludismé, Paludienne, Fièvre Paludisme, Fièvre Palustre, Fièvre de Marais, Fièvres Malariques, Fièvre Tellurique. *Ital.*—Malaria, Paludismo, Febbre Intermittente, Febbre Malarica, Infezione Malarica. *Hind.*—Bookhar, Jara Bookhar, Monsum ki Bookhar; *Beng.*—Jhor, *Goorkh.*—Tap.

Definition.—Malaria is the condition produced by infection with the Plasmodia described. The term *malaria* [1] is used to include a class of diseases which occur both endemically and epidemically, and which, clinically, ætiologically, and therapeutically, exhibit much similarity. The main group of malarial diseases are the malarial fevers, which show a marked periodicity, and are characterised by paroxysmal intermittent fever, anæmia, enlargement of the spleen, melanæmia with deposition of pigment in internal organs, with a tendency to relapses, and finally, if the paroxysms continue, to the production of a specific cachexia. Quinine properly given cures these fevers.

Incubation period.—This has been determined by direct inoculation of malarial blood, by experimental production of malaria from infected mosquitoes, and by observations after persons have been only one day in a malarious place.

The period of natural incubation is variable, the variations being within wide limits, the conditions upon which those variations depend are as yet only very imperfectly understood. The average incubation period of benign tertian malaria is eleven days, of quartan fourteen days, and of malignant tertian six days.

The length of the incubation period varies mainly with the species of parasite involved, the number of sporozoites injected when infection occurs and the resistance of the patient, that is, the effectiveness of the defensive agencies operating in his economy, and probably other unknown causes. It is considered that a certain proportion of parasites to red blood cells is required to bring about a paroxysm. In a very severe paroxysm 20 per cent. or more of the red cells may be infected, in a moderately acute paroxysm there may be 10 per cent., and in a mild attack 2 per cent. Naturally the higher the proportion of erythrocytes infected the greater the amount of toxin liberated with sporula-

[1] The term *malaria*, although Italian in origin, was introduced by MACCULLOCH in 1827 as a substitute for the more limited designations "paludal poison" and "marsh miasm."

but each also settles down to grow, sporulate and rupture its host-cells at the same time, due probably to the fact that the toxins liberated may kill off immature forms, or stragglers, in small numbers, being easily dealt with by phagocytosis."

Sweating stage.—At first there is mere moisture of the skin. The sweating usually begins about the head and is soon general. Beads of sweat appear on the forehead, chest and hands; often this is followed by a drenching perspiration. The temperature falls to normal, and finally to one or one and a half degrees below normal, and the patient feels comparatively free from discomfort, sleep often overtaking him in the middle of the sweating stage. Then the sweating ceases. The urine still continues scanty and high-coloured. This stage lasts from two to four hours. The attack often passes off about midnight.

The paroxysms usually come on every second day (benign tertian and malignant tertian), or third day (quartan), or daily (double benign tertian, double malignant tertian, triple quartan); they are subject to various modifications, some of which occur as ordinary events, others being unusual and abnormal.

A continuous or remittent temperature may arise from a prolongation of the paroxysm (due to malignant tertian parasites) or to absence of simultaneous sporulation, or to unusual susceptibility of the patient to the effects of the toxins. In such cases the second paroxysm begins before the first has ceased.

The numerous clinical phases which malignant tertian fever assumes in India suggest that there may be more than one form of malignant parasite, although only one has so far been discovered.

Some authorities consider that the rigors, vomiting, headache, etc., are manifestations of an anaphylactic process.

Mixed infections.—When more than one species of malaria parasite is going through its life-cycle in the blood at the same time, we call the condition *mixed infection*. Mixed infections are not infrequent, the commonest being that of malignant tertian and benign tertian. Of 1,900 cases examined by the writer by thin smear during 1909 this form of mixed infection was found in 17 cases, or about 0·9 per cent. Among Indian troops in 1922, of 11,010 cases of malarial fever diagnosed microscopically, in 3,477 *fresh* infections there were 0·46 per cent. of mixed infections, and in 8,533 relapse cases there were 0·02 per cent. Of 8,152 British troops diagnosed as malarial fever microscopically there were 0·15 per cent. of mixed infections in fresh cases and 0·33 per cent. in relapse cases. They are most common at the height and latter part of the malarial season. Mixed benign and quartan occur, but are rare except in quartan districts (see Tables, pp. 13 and 14). In these mixed infections the clinical picture, especially the temperature chart, will vary very much. We may have daily paroxysms, or remittent, or almost continuous high, temperature, giving a clinical course which may simulate that of other forms of infectious fevers. The finding of malaria parasites in the blood decides that malaria is present, but other infectious disease may also be present; their detection in India never absolves from the need of determining whether some other disease is not also present. Mixed infections are probably more numerous among children than adults.

Sporulation and clinical symptoms.—The different stages and clinical manifestations of malaria can be correlated to the stages of development of the parasite in the surface blood. As the cold stage approaches, the pigment gathers near the centre of the parasite and sporulation begins. During the shivering fit the red cells are rupturing and the parasites are breaking up, setting free into the peripheral blood (and elsewhere) toxins and spores.

more or less violent accompany the cold sensations, beginning with the muscles of the lower jaw and extending to the extremities and trunk, so that the body shakes all over, the teeth chatter, the skin is pale or bluish, the expression is changed, there are dark rings under the eyes, the features are sharp and pinched, the skin shrunken, and the so-called "goose-skin" appearance is produced. The patient feels intensely cold and piles over himself a heap of bed-clothes even in the hot weather. The nails and lips are blue. He lies in bed all huddled up. The pulse is small, hard and increased in frequency, the breathing is hurried; headache may be very severe, and if he gets up he feels giddy. There is often vomiting. The temperature, though low on the surface, is high in the mouth and rectum. The urine is pale, in large quantity, of low specific gravity, and frequently discharged, partly at least owing to the contraction of the peripheral vessels and consequent rise of renal blood pressure, with hyperæmia of the kidneys. An increase of urea begins some hours before the paroxysm, is at its maximum at the end of the rigor, and decreases in the hot and sweating stages, though remaining still high. The urine generally contains urobilin and urobilinogen. This stage usually lasts from a few minutes to half an hour, but it may go on for an hour or more; at the end of it the temperature may be 102° or higher. The cold stage is more marked in simple quartan and benign tertian ague; it is less marked, and sometimes even absent, in malignant tertian fever. In young children the rigor may be replaced by, or the hot stage accompanied by, convulsions. The heat output is lessened; the causative metabolic changes are but little known.

Hot stage.—This may set in gradually or suddenly. There is at first a feeling of relief from the misery of the rigors and cold stage generally. The temperature continues to rise and may attain its maximum about two hours after the commencement of the paroxysm. As the temperature goes up the shivering lessens and is replaced by flushes of heat throughout the body. The skin now becomes hot, pungent and flushed; the tongue is dry; there is often vomiting and much thirst; the headache is more severe, the pulse is full, bounding and rapid. The blankets or heavy clothes are thrown off. The temperature varies from 102·5° to 105° F. or higher. The breathing is accelerated, and vomiting, if it was present, continues. This stage lasts a varying length of time, being 3–4 hours in quartan, 4–5 hours in benign tertian, and 16–20 hours or longer in malignant tertian. The urine is scanty, high-coloured, and sometimes contains albumin; there is an increase in the acidity and urea; a trace of hæmoglobin is frequently found.

The spleen may become palpable, and there is often pain on pressure over the left costal arch; in some cases pain is felt when the tip of the finger is drawn along the left lower intercostal spaces. If the attacks continue to recur the splenic enlargement may be more or less permanent. The hot stage is present in the vast majority of cases; it may be absent in those who have acquired some degree of immunity.

In some cases the subjective symptoms are nothing more than a slight feeling of chilliness without pyrexial disturbance, little or no headache, no nausea or sickness; the attack is so mild that the patient does not go to bed, although the temperature may be 101° to 102° F. or higher. These cases may occasionally become dangerous by developing pernicious symptoms; this is predisposed to by the patient moving about. On the other hand, a slight rise of temperature may be associated with distressing headache, vomiting and prostration. It is possible that the malarial toxins are complicated bodies, varying in composition. There is also, in all probability, individual idiosyncrasy to their action. "Each type of parasite may cause irregular symptoms at first,

Single infections.—In single infections each paroxysm is due to the brood of the parasites that caused the preceding paroxysm. For example, if a simple or malignant tertian paroxysm occurs on a Monday, the spores it sets free will infect the red cells and give rise to the next attack on Wednesday, and so on.

Double and triple infections.—In this condition we have two or three groups of parasites of the same species which do not sporulate at the same time. In the case of simple and malignant tertian, one generation would sporulate, say, on Monday and Wednesday, and the other on Tuesday and Thursday, and so on on alternate days. Triple infections may also occur, there being three groups of the same species of parasite in the blood at the same time; in triple quartan infection the paroxysms would occur daily, and in the case of simple and malignant tertians somewhat complex forms of febrile paroxysms are liable to be met with.

It is obvious, therefore, that a daily fever may arise from double infection of simple or malignant tertian parasites, or a triple infection of quartan parasites. When this occurs it is usually observed that the paroxysm of one day is either more pronounced or less marked than that on the following day, showing that one group of parasites is playing a dominating rôle in the blood.

Ambulatory cases.—These are cases in which the symptoms of the paroxysm are so slight that the victims go about their work as if they were well It is very often met with in the Army in India during the malaria season, when quinine is being regularly issued as a prophylactic, frank paroxysms being prevented by the drug. But it occurs in cases that have not taken quinine, *e.g.* in bazaar and village children. It is also common among British officers and soldiers at duty. The writer has suffered from this condition several times. Any symptoms that arise usually last only for a few hours on the day they are due—malaise, headache, a feeling of chilliness, some pains in the limbs and body, slight rise of temperature, which will vary from 99·5° to 101° F., coming on usually some time in the forenoon. During one series of these mild attacks in Basra in March, 1915, the author's blood showed a moderate infection of benign tertian, schizonts and gametes. He had been taking the usual prophylactic, 5 grains of quinine daily for six days in the week, and 10 grains on Sundays; obviously this quantity was insufficient. Thirty grains daily for three days and 10 grains daily for a month, followed by 5 grains daily for two months, eradicated the infection.

In all endemic regions in India abortive attacks of malaria occur in large numbers of people. They suffer from a mild attack of fever, and in most instances rightly, put it down to malaria, take large or small doses of quinine for some days, and the evidences of the infection for the time being pass off. Practically all these ambulatory cases are malaria-carriers.

The ordinary case of malaria seen in people dwelling in endemic areas is one in which there have been infection and re-infection several times each year, and year by year; in most cases several infections have been superimposed. These cases acquire a certain degree of relative immunity. Further, the clinical course of these cases need not show the clear-cut and well-defined symptoms which occur in paroxysms of primary infections. There are in them many irregularities, affecting one or other or all three stages of the paroxysm, and the total duration may be shorter. A visit to a ward containing, say, a dozen of these relapsing patients will show that there are few temperature charts quite identical. Lt.-Col. S. P. JAMES, I.M.S.,[1] gives some charts from these cases, with the clinical history of each; these form a large percentage

[1] *Malaria at Home and Abroad* and his article, "Malaria Symptomatology," in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. II, pp. 1591–3.

When the rigor ceases, and while the hot and sweating stage lasts, the young parasites of the next generation, and pigmented white cells, with pigment liberated by the breaking up of the fully developed schizont, can be seen under the microscope. During the interval the parasite is growing in size, becoming pigmented and developing. As the parasites are in the red cells during the apyrexial interval, obviously it is not their presence that brings about the paroxysm; the fever must be due to pyrogenetic toxins set free into the plasma when they are liberated. Hence in remittent and continued paroxysms segmenting parasites are met with at all stages of the fever.[1]

In all forms of malarial fever the first paroxysms are liable to be prolonged beyond the average periods mentioned above, possibly because parasites do not at first all sporulate together, but in successive groups, thus maintaining a longer discharge of toxins into the blood plasma. It is possible also that in the early attacks the person infected is more sensitive to the effects of the toxins. For these reasons a simple tertian paroxysm may continue until the next is due, giving the case some of the ordinary characters of malignant tertian fever; whereas later the attacks become frankly tertian. So mild are some attacks that people do not stop work on their account: children are often seen playing about in bazaars with a temperature of 100° F. or higher while going through a paroxysm. Typical sub-tertian with reference to each paroxysm may be considered as being as truly intermittent as ordinary benign tertian and quartan; when the fever is remittent or continuous, it is simply the result of succeeding paroxysms running into one another without any intermission.

We may have all kinds of combinations of malaria parasites in the blood at the same time, giving rise to a curious arrangement of the paroxysms, some of which, even when we know what is going on in the blood, are very puzzling.

It is not often that we get a serious deviation from the clinical type in benign tertian and quartan, but in malignant tertian this is quite common.

The diversity of clinical forms that may be assumed by atypical paroxysms should be borne in mind, and in any case of "fever," no matter what the symptoms, blood examination for malaria parasites should be carried out. This is a *cardinal rule, although, as noted, malarial infection is frequently present* concurrently with other maladies.

Injections of blood containing the benign tertian parasite in cases of general paralysis of the insane give benign tertian fever. Great amelioration of the clinical *manifestations of general paralysis occurs, possibly attributable to the "protein* shock" produced. This procedure has led to the acquisition of much information regarding the behaviour of the benign tertian parasite within the body and its clinical effects. "After numerous 'passages' without the intervention of the mosquito host, the parasites can be found in large numbers in the blood stream without having altered in any way in character or in virulence. Furthermore, contrary to the opinion formerly held, it has been shown that inoculation of sporozoites from the salivary glands of one infected Anopheles [on one occasion] will produce in some persons *quotidian* rigors, due to parasites sporulating within a day of each other. In many cases also, after an incubation period of seven to ten days, the onset of the malaria attacks is characterised, not by typical intermittent fever, but by a *remittent* fever, which may persist for a week or more before becoming frankly intermittent."[2]

Multiple infections.—When more than one generation of the same species of parasite is going through its life-cycle in the blood at the same time, we have what is called *multiple infection*. As has just been indicated, this term is now known to be somewhat of a misnomer, since the condition does not necessarily imply that there has been infection through more than one mosquito bite.

[1] MANSON'S *Tropical Diseases*, 8th Ed., p. 35. [2] *Ibid*, pp. 37, 38.

are seldom pronounced premonitory symptoms; the attack sets in abruptly, the shivering fit, which is very seldom absent, is well marked and associated with much discomfort, the fever is usually high, the temperature going up to

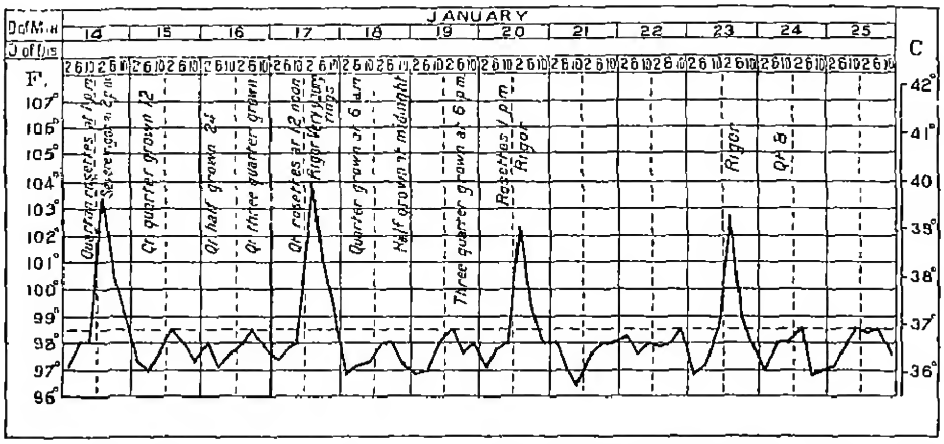


Fig. 62.[1]—Infection with one group of *P. malariæ*. No quinine treatment. Commencing with the stage of very young rings at 2 p m on the 17th, follow the growth of the parasites to the state of rosettes at 1 p m. on the 20th. Note the finding of rosettes about an hour before the commencement of the rigor.

103° to 105° F. or more, and the sweating is profuse. All three stages are well defined. Quartan has the longest cold stage, but on the whole the paroxysm is the shortest of the malarial fevers. Irregularities in the fever are seldom met with; it is usually sharp and its stages clear-cut, and except in areas in which it predominates it is seldom associated with malarial cachexia (Figs. 61, 62).

The clinical course of quartan will naturally be determined by the ages of the parasites in the blood. Where they are all of the same age it will be a typical attack, and we get a simple quartan fever (*quartana simplex*); when of different ages there will be attacks on two of each three days (*quartana duplex*) (Fig. 63), or on all three days (*quartana triplex*). The writer has never seen the last.

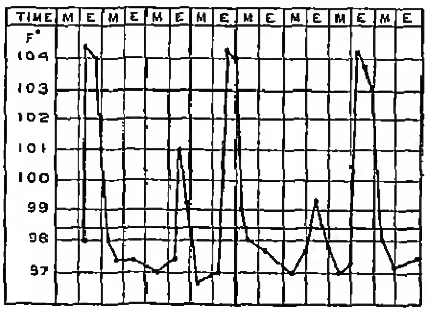


Fig. 63.—Double Quartan.
From Daniels and Wilkinson's *Tropical Diseases and Hygiene*, Vol. I.

While chronic quartan malaria is difficult to eradicate, ordinary quartan infection seldom produces symptoms dangerous to life. Its persistence was known to the Ancient Romans, among whom some such phrase as "may the quartan seize you" was sometimes used as a wish for ill luck to befall the person addressed. The cause of the irregular and scattered geographical distribution of quartan malaria in India is not known.

For description of the parasite of quartan fever see p. 162 *et seq.*

[1] From Lt.-Col. S. P. James's article, "Malaria. Symptomatology," in Byam and Archibald's *Practice of Medicine in the Tropics*, Vol. II.

of those treated in civil and military hospitals in India and are deserving of close scrutiny.

Effects of the improper use of quinine.—The most frequent cause of the atypical course of paroxysms is insufficient or improper quinine treatment. If we take four-hourly charts of a primary untreated malaria case we find that after a certain number of paroxysms a regular intermittency is established. On the other hand, if such a case is treated irregularly with inadequate doses of quinine this regular intermittency is not developed. This is a common experience. The fever may then run on for an inordinate time.

THE ORDINARY FEBRILE TYPES

There are three varieties of malarial fever in India, viz. *Quartan; Simple* or *Benign*[1] *Tertian*, and *Malignant* or *Sub-tertian*, each being caused by corresponding parasites which invade the red cells.[2]

Simple tertian and quartan malarial fevers were formerly grouped under the

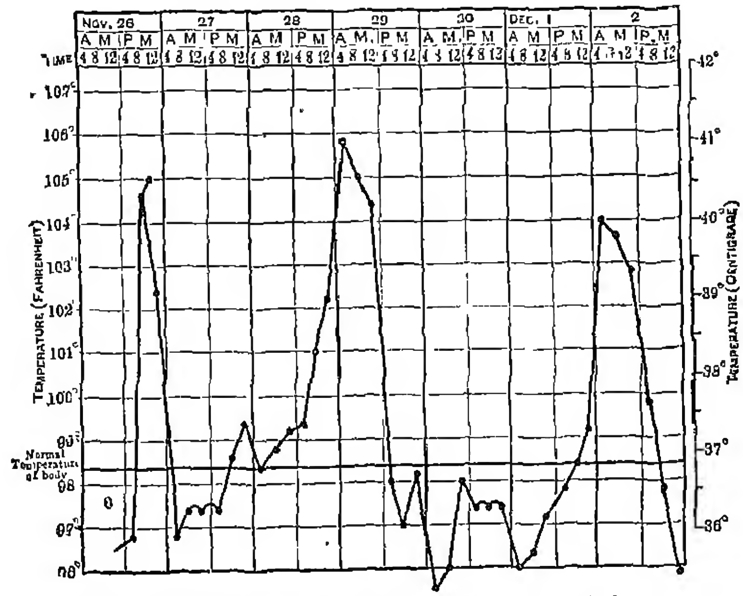


FIG. 61.—Quartan ague. Very definite quartan periodicity. From MANSON's *Tropical Diseases*, 8th Ed.

common term *ague* or *intermittent fever*. This is inaccurate for several reasons. Malignant tertian fever used to be called *remittent fever*, a term which is also inapplicable, as many of these cases are quite intermittent.

The quartan paroxysm.—The incubation period averages from fourteen to eighteen days. The paroxysm usually lasts from eight to ten hours. There

[1] It is worth mentioning that the term "benign" applied to simple tertian infection is not altogether accurate, for though the febrile paroxysms associated with it are but rarely dangerous to life itself, its parasite may cause considerable and abiding disability. The strong tendency to relapse of the paroxysms and the difficulty with which the parasites are eradicated by quinine therapy indicate how inappropriate is the application of the word "benign" to this infection (see pp. 186, 187).

[2] The *quintans*, *sextans* and *septans* of the ancient writers were in all probability relapses.

approximately the same or of different ages. If they are of the same age we get typical attacks of simple tertian (*tertiana simplex*). In many cases the fever is quotidian—a pyrexial attack occurs every day (*tertiana duplex* or double benign tertian). This is due to the coexistence of two generations of the parasite maturing on alternate days. Sometimes the double character of the infection is obvious clinically, as the pyrexial attacks vary in severity, being alternately severe and mild (Fig. 66). In a double tertian the more frequent recurrence of the pyrexia causes more rapid development of anæmia and debility, and the prognosis, therefore, is more serious.

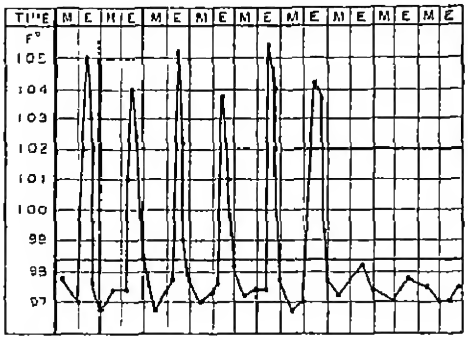


FIG 66.—Double benign tertian. Daily paroxysms definitely developed.

From DANIELS and WILKINSON'S *Tropical Medicine and Hygiene*, Vol I.

In benign tertian infection occurring during epidemic malaria, very commonly several broods of different ages are in the blood, giving rise to irregular sub-continuous fever.

When perniciousness occurs in benign tertian malaria the author believes it is usually due to the large amount of toxins set free by a vast number of parasites in the blood; sometimes, however, there is coexisting malignant tertian infection. The perniciousness, as a rule, takes the form of hyperpyrexia, often associated with cerebral symptoms of the comatose type. On the other

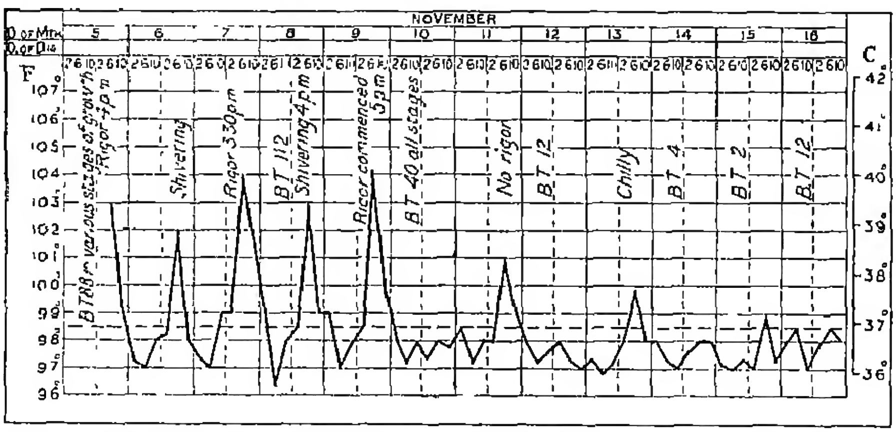


FIG. 67.—Infection with various groups of benign tertian parasites. No quinine treatment. Note (1) the large number of parasites, (2) the regular daily febrile paroxysm cannot be correlated with the stages of growth of the parasites; (3) the febrile paroxysms ceased although no quinine was given; (4) the parasites did not entirely disappear from the peripheral blood.

From Lt.-Col. S. P. JAMES'S article, "Malaria: Symptomatology," in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. II

hand, intense malarial intoxication may be met with in cases where few parasites are to be found in the peripheral blood.

The vast majority of cases of malaria in India consist of simple tertian,

The simple tertian paroxysm.—This usually lasts from nine to twelve hours. Before the initial paroxysm there are often premonitory symptoms for several days, and a remittent type of fever is frequently present at that time. The shivering fit is, as a rule, less severe, and the fever more marked and prolonged, the headache, vomiting and pains in the bones more distressing, than in quartan. In the hot stage the fever, 102·5° to 104° F. or higher, *for a period varying from three to six hours*, is followed by the sweating stage (Fig. 64); the forehead and head generally, neck, body and extremities ooze sweat in large quantities; the pulse is slower, temperature falls by crisis, and the patient goes to sleep still sweating. He wakes up feeling comparatively well, and remains so during the interval.

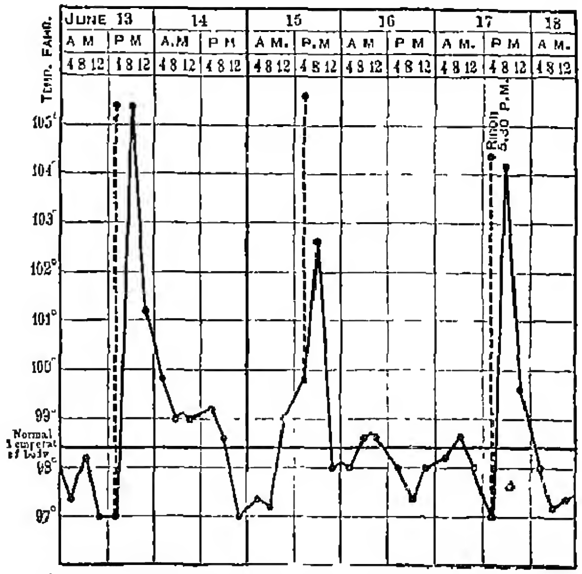


FIG. 64.—Typical temperature chart of benign tertian ague. Definite and regular periodicity.

From MANSON's *Tropical Diseases*, 8th Ed.

The clinical course is in accordance with whether the parasites are all of

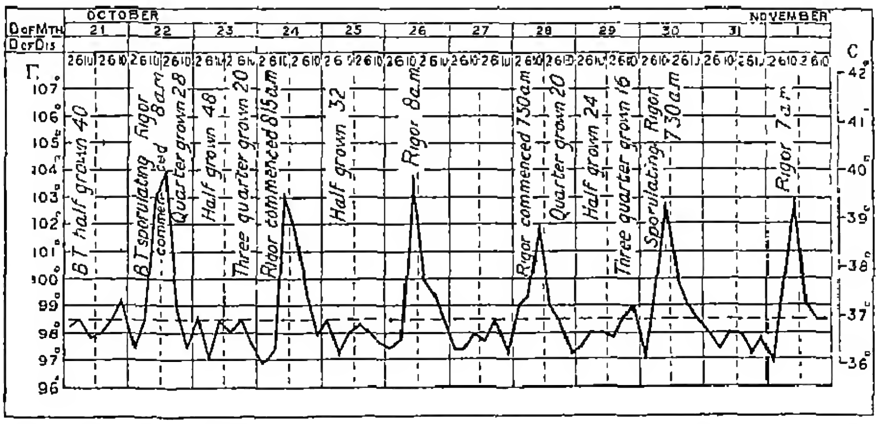


FIG. 65.—Infection with one group of benign tertian parasites. No quinine treatment In examining the chart, note the following points · (1) The rigors began at approximately 8 a.m until the 28th, when they commenced to " anticipate " by about half an hour, (2) the course of the temperature can be correlated with the three stages of growth of a parasite which takes forty-eight hours to complete its cycle; (3) sporulating forms were found about an hour before the rigor commenced, (4) the fever rises very suddenly, but falls less suddenly; (5) B T. 40 means that 40 benign tertian parasites were found in 100 fields of the microscope.

From Lt Col S. P. JAMES's article, "Malaria: Symptomatology," in BYAM and ARCHIBALD's *Practice of Medicine in the Tropics*, Vol. II.

and keeps up for many hours, then there is a temporary fall, called the *pseudo-crisis*, after which the fever increases again, rising higher than it was previously, and finally drops to well below the normal crisis (Fig. 69). Probably two broods of sub-tertian parasites are running their life-cycle concurrently, one of which matures later. The other symptoms are usually very severe, but the shivering fit is more often absent or decidedly less marked (and may consist of merely chilly sensations) than in other malarial fevers. Sometimes, however, it is severe and prolonged, or, after the occurrence of several paroxysms, shivering or even chilliness may be absent. The temperature usually ranges between 100·5° and 102·5° F., but in many cases goes up to 103° F. or over. The temperature may, however, run very high. The hot stage may last from sixteen to twenty hours, with usually minor remissions of the fever during this time, and may be followed by profuse sweating. This stage may be associated with a tendency to the adynamic state, with vomiting, bilious or watery diarrhœa, severe headache, anorexia, pains in the limbs and depression. On the other hand, sweating may be intermittent, with hot, dry intervals. The whole attack may last from twenty-four to forty hours, so that the interval, seeing that the cycle is forty-eight hours, must be short. There may be jaundice. If unchecked by quinine, loss of strength may rapidly set in. The fever is associated with a coated tongue, and bilious vomiting often occurs. There may be pain in the "pit of the stomach" with tenderness from the vomiting, complete loss of appetite, thirst, and constipation or diarrhœa. The kidneys are often more or less implicated, as indicated by either albumin, casts or renal epithelium in the urine; they are much less frequently affected in simple tertian and quartan. Malignant tertian fever is specially characterised by its disposition to irregularity, and to the production of a remittent or continuous fever, and by the frequency with which symptoms of a pernicious type develop. The remittent or continued type of the fever in all probability is due to the grouping of the parasite in the blood, the segmentation of which in the red cells extends over comparatively long periods of time, creating paroxysms of long duration, which, from their peculiar tendency to anticipation and retardation, run into one another, hence the term *remittent* fever applied to it last century, a term which is for many reasons inappropriate. (See Fig. 70.)

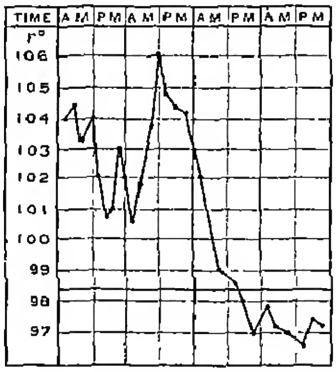


FIG. 69.—Severe sub-tertian malaria (treated) Crisis after quinine.

From DANIELS and WILKINSON'S *Tropical Medicine and Hygiene*, Vol I.

All cases of malignant tertian fever should be considered severe, in contradistinction to the simple and quartan types, which, except during periods of epidemic malaria, may, as a rule, be classed as *mild* or *benign* types of malarial infection. Although but few cases of malignant tertian fever are fatal, and the vast majority are readily amenable to proper treatment by quinine and other means, and some are cured spontaneously, it is undoubtedly the case that the largest percentage of pernicious malarial attacks arises in connexion with malignant tertian, and every case showing the presence of malignant tertian parasites in the blood should be considered as serious in nature and treated accordingly. It may be associated with very grave symptoms coming on suddenly and ending fatally, hence the term *malignant tertian*. Blood examination should be made at least daily.

which has hitherto been considered to be the easiest form of malarial infection to eradicate from a locality and from infected persons. This does not correspond with the experience of many experts in India. Notwithstanding statements to the contrary, the largest number of relapses occur in cases of simple tertian fever. For many years the writer had opportunities of watching and following relapses in localities where there is no initial malaria. He found that 79 per cent. of these were simple tertians, 20 per cent. malignant tertians, 0·5 per cent. quartans, and 0·5 mixed benign and malignant tertians. The statement that perniciousness is confined to malignant tertian infections is also opposed to the writer's experience, for he has met with such conditions as algid paroxysms, cerebral attacks, choleraic attacks, secondary malarial pernicious anæmia and hyperpyrexial phenomena associated with simple tertian infection, while a small proportion of cases of repeated simple tertian relapses or re-infections end in chronic malarial cachexia. In discussing the subject with medical men of wide experience of Indian malaria, it is ascertained

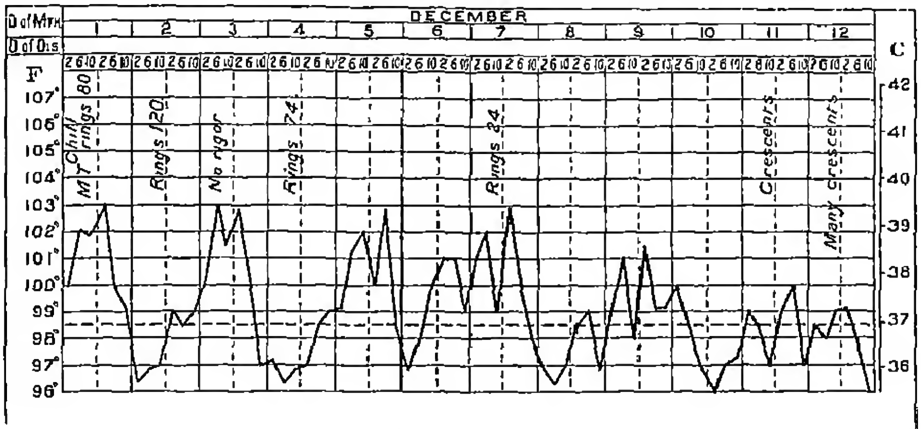


FIG. 68.—Typical infection with malignant tertian parasites. Note (1) rings 120 means that 120 parasites, all in the "signet ring" stage, were found in 100 fields; (2) for the first few days the chart is definitely tertian in character, (3) the febrile paroxysm lasts a long time (about eighteen hours); (4) the switchback character of the fever, especially on the sixth and seventh days; (5) the appearance of crescents on the eleventh day.

From Lt.-Col. S. P. JAMES's article, "Malaria: Symptomatology," in BYAM and ARCHIBALD's *Practice of Medicine in the Tropics*, Vol. II.

that the author's experience in the above respects is not exceptional. It is interesting to state that the foregoing paragraph was written sixteen years ago. The grave importance attaching to benign tertian infection was verified by the experience of the Great War. It is difficult to eradicate once it has reached the chronic relapsing stage, and long-continued treatment is indispensable to effect this within a reasonable time.[1]

For a description of the parasite of benign tertian fever see p. 164 *et seq.*

The malignant tertian paroxysm.—Syns.: *Malignant Tertian, Subtertian, Crescent Fever, Tropical Fever* and *Tropical Malaria.* These are terms given to the third form of malarial fever met with in India. The paroxysm lasts from thirty to forty hours or longer. It is the most severe form of malarial fever, and represents a more profound degree of intoxication than do the more innocent forms of malarial infection. The temperature chart is quite distinct from the other forms of malarial fever (Fig. 68). The temperature rises rapidly

[1] The Author in *Proc. Ind. Sc. Cong.*, 1918, p. 89 *et seq.*, and *The Lancet*, 1918, ii, p 151.

these cases there is grave depression, dry tongue, mild or muttering delirium, *subsultus tendinum*, drowsiness and apathy; the abdomen is swollen and tender, and the spleen and liver are enlarged. These cases are very fatal if not speedily recognised, but early diagnosis, proper quinine treatment and good nursing will save the great majority of them. If treated as real enterics they gradually sink. The first steps in all such cases should be to examine the blood microscopically, make cultures of the blood and, later, carry out the Widal test; these nearly always lead to a correct diagnosis. The blood examination must be thorough, and should include stained and fresh preparations and, if necessary, a thick film. On finding malaria parasites quinine should be injected intravenously at once. The change for the better in the patient's condition under this treatment will be speedy and surprising, if he is not already beyond hope of recovery. These are cases of malarial toxæmia, in which the amount of the poison overwhelms the system; they are common during epidemic malaria. Although in most cases the prognosis is good, the mortality is comparatively high. It should be borne in mind that the double infections of enteric and malaria occasionally occur (see pp. 196, 197).

Adynamic remittent.—This is also a grave form of malignant tertian fever. It is associated with restlessness, depression, trembling of the hands and tongue, and heart weakness; serious and rapid destruction of red blood cells is taking place, there is jaundice, a tendency to syncope and sometimes hæmorrhages. Some coexisting infection, such as syphilis, tuberculosis or alcoholism, is often the deciding factor in producing adynamic and typhoid remittent. The remarks on early diagnosis and prompt quinine treatment made regarding typhoid remittent hold good in this form also.

Pernicious attacks, which may occur in all types of malarial fever, are dealt with separately.

For description of the parasite of malignant tertian fever see p. 166 *et seq.*

Pernicious Attacks

Definition.—When malarial infection is very intense, or has continued for some time, it may suddenly lead to symptoms which endanger life, and specially affect one or more internal organs. These symptoms vary considerably, and are spoken of as *pernicious attacks.* They are, as a rule, rare, and occur in the most malarious places at the most malarious period of the year; but during *epidemic malaria* and hyperendemicity they are very common.

While pernicious attacks may occur in infections with all species of parasite, they are specially prone to do so in that with *P. falciparum*, during periods of severe malarial epidemicity, after a series of apparently normal paroxysms, and in people whose stamina is lowered from one or other cause, especially starvation, alcoholic intemperance and excessive fatigue. They are always extremely dangerous to life and come on suddenly, often unexpectedly, and unless promptly and vigorously treated are likely to be fatal.

Perniciousness is usually preceded by a notable increase of parasites in the peripheral circulation. Other possible signs of approach are—the occurrence of an extremely large number of young parasites, of malignant segmenting forms, and a high proportion of multiple infection of individual erythrocytes. When multiple infection of red cells exceeds 5 per cent. of the infected cells, or over 200,000 parasites per cubic millimetre, urgent and immediate treatment by quinine intravenously is indicated. Though not confined to it, pernicious symptoms generally develop during the later half of the parasites' cycle in the blood. The chief forms of pernicious attacks are given below.

Hyperpyrexial pernicious attack.—This is a serious complication, the

After the paroxysms have subsided the patient is usually somewhat prostrated, whereas a few paroxysms of benign tertian or quartan fever do not, as a rule, seriously affect the patient's strength and condition. It is a serious mistake to attempt to fight malignant tertian fever by going about with it doing ordinary work. "Some people try to walk off a fever; many of those who do so literally walk to the grave." This is especially the case in India with regard to typhoid fever and malignant tertian fever. In all cases of malarial fever recovery is retarded by any attempt at getting up and going about in the ordinary way.

The mortality of sub-tertian fever is higher than in the other types of malarial fever It is accompanied by great and rapid destruction of red cells, and when severe and prolonged it may be followed by acute malarial cachexia (p. 202); this is the most frequent cause of the acute malarial cachexia occasionally met with in our European troops, especially during epidemic malaria.

It is curious that this parasite may continue in the blood stream for weeks consecutively, especially in native children in the autumn malarious season, without causing definite paroxysms or any serious pyrexial manifestations, and in this circumstance it may gradually produce anæmia, enlarged spleen, œdema of the feet and digestive disturbance.

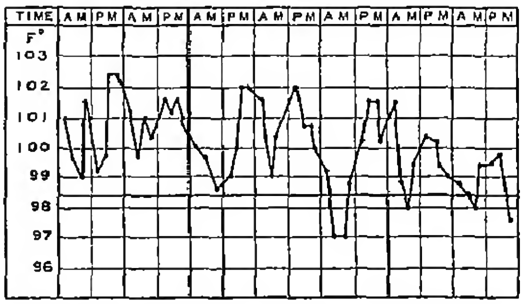


FIG. 70—Sub-tertian malaria. Periodicity indefinite.

From DANIELS and WILKINSON'S *Tropical Medicine and Hygiene*, Vol. I.

Plasmodium falciparum appears to bring about a stickiness of the infected erythrocytes and *to produce some adherence to* the capillary walls of the organs in which they sporulate. The *troubles which arise have been* attributed either to a mechanical blocking of the capillaries or to the intense local action of the toxin, or to both these causes, in the same victim. As a consequence we may have pernicious manifestations of malaria, varying according to the organ mainly affected. For example, if it occurs in the brain it may cause coma, convulsions, paralysis; in the pancreas hæmorrhagic pancreatitis.

There are certain groups of symptoms frequently met with in sub-tertian fever giving rise to definite clinical forms of the disease deserving of special mention; the following are among the chief of these groups.

Bilious remittent fever.—This is a common form of sub-tertian malaria, associated with persistent bilious vomiting and diarrhœa, which recur with each paroxysm; there is a certain amount of jaundice, due probably to bilirubin in the blood or deposited in the skin, mucous membranes and sclera. These attacks, though seldom fatal, are often severe; there is no interval during which the temperature is normal, merely a remission occurs, hence the use of the old term *bilious remittent fever.* Usually the temperature is not high—101–102 5° F. These attacks often lead to serious anæmia, debility and prolonged ill-health.

Typhoid remittent.—One of the commonest forms of severe sub-tertian attack is that which simulates enteric fever, and in which no system is specially involved, the patient after a week or so (sometimes sooner) passing into the "typhoid state," *the temperature having varied from* 102° to 104·5° F. In

Gastro-intestinal attack.—These arise from the capillaries of the mucous membrane of the intestinal tract becoming blocked with malaria parasites. In the ordinary attack the usual symptoms are nausea, vomiting, diarrhœa and jaundice. It may take one of several forms—*gastric, dysenteric, melænic, bilious, choleraic*, etc.

In the *gastric form* there are severe pain and tenderness in the epigastrium, constant vomiting, often hæmatemesis, and retracted abdomen.

In the *dysenteric form* there are the usual symptoms of dysentery—frequent evacuation of blood and mucus, griping and straining, occurring during a very severe paroxysm of malaria.

In the *melænic form* the only symptom may be the discharge of dark-looking tar-like blood, or of red blood in the stools, the volume of which may be very large.

Bilious attack.—This is reasonably to be explained as the result of the great destruction of red blood cells, the hæmoglobin of which is taken up by the liver and transformed into bile. The chief symptoms are vomiting and purging of bilious material, jaundice, high temperature, with a tendency to coma and death, though there may be slow recovery.

Choleraic attack.—The paroxysm is associated with copious vomiting, severe watery diarrhœa, the stools and symptoms simulating true Asiatic cholera; the stools, however, always contain some bile, while the rice-water stools of genuine cholera do not. The skin is cold and clammy, pulse thread-like or absent at the wrist, temperature subnormal; the voice, though weak, is not the harsh, high-pitched whispering of true cholera. There is suppression of urine and cramps in the abdomen and legs. Grave uræmia may soon set in with thready pulse, delirium, convulsions, coma and death. This form of perniciousness is very fatal if not diagnosed early and treated promptly with quinine.

The choleraic type is met much more commonly in some parts of India than in others, *e.g.* it is in some years almost epidemic in the Peshawur Valley. True cholera and malaria may coexist in the same patient.

Pancreatic perniciousness.—The onset is acute, with agonising pain in the upper part of the abdomen, signs of partial intestinal obstruction, followed by profound collapse. The writer has treated half a dozen of these cases (all fatal), and when pathologist to the Afsul Gunj Hospital, Hyderabad (Deccan), performed post-mortems on eleven cases. Clinically they are always puzzling. There is usually hæmorrhage into the pancreatic substance and patches of melanin in the tissues of the gland; the capillaries of the organ may be choked with infected red cells.

Suprarenal perniciousness.—The adrenals are occasionally attacked in severe infection. The characteristic signs are—marked muscular prostration, low blood pressure which is continuous, vomiting, diarrhœa, pain in the lumbar region, headache, delirium, passing into coma and death. There is some difference of opinion as to the real cause of these symptoms. In heavy malignant tertian infections the most constant change in the suprarenal capsules found by DUDGEON and CLARKE is a decrease in the fatty lipoids of the cortical layers. "The chromaffin content in the cells of the medulla was diminished. In five of the thirty-five cases thrombosis of capillaries with hæmorrhages into the gland, and degenerative changes in the cortex with and without blocking of the blood vessels, were also present. In these five cases there was also a massing of parasites in the capillaries of the brain, and this, in all probability, was the pathogenic basis of the symptoms, at least as regards those referable to the

sole cause of the patient's condition being a surcharging of the system with toxins which have caused a rise of temperature, ranging from 106° to 112° F. There may be a brief stage of wild delirium, followed by muttering, unconsciousness, coma and death in a few hours. Some of these cases were, in former times, called "thermic" or "ardent fever." In *the great majority of them no* morbid change is found in the organs or tissues; there would appear to be an acute *malarial toxæmia*, which is specially common in epidemic malarial years.

Cerebral pernicious attack.—These are usually caused by the overloading of the blood vessels of the brain with malaria parasites which have accumulated in that organ. There are several special forms of it, the chief being the *comatose form*, in which there is severe headache, confusion and stupor or delirium, scanning speech, weakness, sleepiness, disturbance of vision, these symptoms coming on rapidly. There are involuntary evacuations of urine and motions, quick and thready pulse, dilated heart followed by coma. In fatal cases the tongue is dry and the body gets colder and colder, but the rectal temperature is high; the breathing is slow and peculiar, and the pupils contracted. There may be a rally and then collapse. Coma may come on without hyperpyrexia, the temperature being usually from 102° to 104° F. The condition may pass off with the crisis, or go on to grave weakness, collapse and death; it tends to disappear under proper treatment, some cases recovering. *There are (usually) parasites in the blood, enlargement of the spleen and* absence of paralysis and of local symptoms. Some delirious cases show trismus, contraction of limbs, opisthotonos, retraction of abdomen, and conjugate deviation of the eyes. These cases often run on to hyperpyrexia. Other forms are—*delirious*, in which there is delirium and excitement, *tetanic*, *paralytic*, etc. In all these the case may end fatally from some secondary lesion days or weeks after the parasites have disappeared from the surface blood under the influence of quinine.

Cerebral malaria may end in delusional insanity, or in one of several forms of psychosis and amnesia.

Embolism of cerebral capillaries occurs in many of these cerebral cases, and the symptoms produced depend upon the region in which the plugging occurs.

Cardiac perniciousness.—The right heart is dilated, there is severe cardiac pain, vomiting of blood, an algid condition and early death. In some of these cases the muscle cells of the heart are laden with malaria parasites. Chronic alcoholics run great risks in exposing themselves to malarial infection

Algid attack.—In this form the blood is usually crowded with parasites, but the ordinary symptoms of the second or hot stage of the paroxysm are absent, the characteristic symptoms being depression, coldness of the breath, sharp nose, shrunken features; lips and extremities cyanotic, skin cold and clammy, pulse small, frequent, soft, compressible and perhaps disappearing from the wrist. The breathing is sighing, slow, shallow and laboured, the voice is feeble, but without the characteristic choleraic huskiness, and there is a tendency to collapse. *Usually the rectal temperature is considerably above normal*, and always some degrees higher than that in the axilla. The algid type may resemble the collapse stage of cholera, but it does not occur in epidemics, the stools are not "rice-watery," do not contain comma bacilli, and always contain some bile; and the blood contains malaria parasites. The patient may die in a few hours.

Hæmorrhagic type.—In this form of perniciousness bleeding takes place from *one or more mucous membranes*—from the lungs, stomach, intestines, kidneys, or from the nose during the paroxysm, but not during the intermission. This variety is rare, but particularly fatal.

diarrhœa, melæna, jaundice, bronchitis or pneumonia, nephritis. To save life in these cases the treatment has usually to be prompt and heroic.

The symptomatology of malarial fevers, especially of coma, delirium, threatened cardiac failure, and other grave clinical manifestations, is, the writer believes, largely due to malarial toxæmia, and is not necessarily connected with changes in the circulation and blood vessels. But this localisation of the effects of the toxæmia is in itself a remarkable phenomenon. To it are possibly due the splenitis and splenic abscess, orchitis, periostitis, neuritis, neuralgias, local headaches, etc., that occur in cases of latent infection—cases which for some unknown reason are often cured by intramuscular injection of quinine after quinine by the mouth has failed.

Of 101 cases with pernicious symptoms recorded, 98 were due to *Plasmodium falciparum* and 3 to *P. vivax*. The dominating pathological and clinical phenomena were—hyperinfection, severe malarial toxæmia and cerebral thrombosis, with large numbers of parasites in the surface blood.

DIAGNOSIS OF MALARIAL FEVERS

The more important points to consider in the diagnosis of malarial fevers are—result of microscopical examination of the blood, periodicity and intermittency of the paroxysms, study of the patient's history, and the quinine or therapeutic test.

Blood examination.—The only accurate and reliable method of diagnosis is *microscopic examination of a specimen of the patient's blood*. All other methods are associated with elements of possible error. It cannot be too repeatedly stated that the finding of parasites is the only justification for a positive diagnosis of present malarial infection; but failure to find them by the ordinary thin- and thick-film methods at any one time does not justify a negative diagnosis (see p. 153). Again, the finding of one species of parasite only does not exclude the undetected presence of other species. On the other hand, while the finding of parasites establishes the presence of malaria, it does not, in a country where it is so prevalent, exonerate from a close search to determine whether this is the only condition which requires therapeutic attention. The discovery of grains or blocks of hæmozoin in leucocytes is also evidence of malaria past or present. Further examination in these cases often reveals parasites. There are fallacies connected with the finding of excess of large mononuclear leucocytes. To be of real value both the total and the differential leucocyte counts must be carried out. While the temperature is rising there is a leucocytosis going on. A definite rise of large mononuclears to beyond 12 per cent. is suggestive of malaria, especially if they are of the macrophagocyte type.[1]

Definite periodicity and intermittency.—This stands next to microscopical examination of the blood as a diagnostic sign of malaria. This periodicity shows itself by recurring paroxysms associated usually with chills, fever and sweating, in the sequence named. When the periodicity is definitely every forty-eight or seventy-two hours there is no doubt about the diagnosis. Quotidian fever met with in liver abscess, pulmonary tuberculosis, various pyogenic infections and other diseases has to be distinguished from double simple and malignant tertian and triple quartan malaria. The rise of temperature in benign tertian and quartan early in the day—usually before 1 p.m.—is helpful; but first paroxysms may come on in the evening if there has been exposure to a chill (Fig. 67). The writer got his first paroxysm of benign tertian malaria in Mesopotamia at 8 p.m. coming down the Karun River from Ahwaz early in

[1] S. P. JAMES, *Malaria at Home and Abroad*, p. 174.

nervous system" (S. P. JAMES).[1] Suprarenal perniciousness may simulate acute peritonitis or appendicitis.

Pulmonary or thoracic type of perniciousness.—A common terminal complication of pernicious cases is pneumonia, usually broncho-pneumonic in type; other cases end with hypostatic congestion of the lungs. There is, however, a true primary perniciousness, marked by rapidity of the breathing, which is difficult, coming on during a severe malarial paroxysm. The pulmonary type may be confounded with pleurisy or with pneumonia, but the changes in the covering of the lungs and in the lungs themselves, as made known by examination of the chest, will clear up any doubt. Examination of the blood is negative as regards malaria parasites in pleurisy and pneumonia, and in pneumonia the sputum may disclose the implicated bacteria.

Perniciousness from malarial anæmia.—In some cases of severe malarial infection the anæmia is intense and progressive. Occasionally this acute anæmia comes on so rapidly and assumes such a serious form that it may rightly be included among the manifestations of perniciousness. The pallor in some of these cases is as intense as that seen after severe blackwater fever or grave post-partem hæmorrhage. These cases are common in epidemic years and years of hyperendemicity, at which times their occurrence can readily be understood; but they are sometimes met with in ordinary endemic years, and not necessarily in heavy infections; then the pathogenesis is not by any means clear. The possibility that malaria parasites have been associated with the almost universal hookworm should not be lost sight of in these cases.

Other forms of perniciousness are—sweating, in which the patient is continuously drenched with an exhausting perspiration; and *syncope,* with a tendency to fainting from weakness of the heart.

Causes of perniciousness.—There are various hypotheses as to the causes of perniciousness. The following appear to be those more generally advanced:

(*a*) A high percentage of erythrocytes being infected and destroyed by malaria parasites;

(*b*) The shedding, by sporulation of parasites, of a large quantity of toxic material owing to the existence of a great number of disintegrating merozoites;

(*c*) Plugging of the capillaries of important internal organs with adult asexual parasites—

- (i) due to sporulating parasites acting as emboli and being too large to pass the lumen of the capillaries;
- (ii) due to degenerative changes or distension with pigment of endothelial cells lining the capillaries;
- (iii) as the result of an ovoid shape on the part of the malignant tertian parasite there is an inability to pass through the capillaries, which the flattened benign parasite can do by infolding (BASS); or
- (iv) resulting from the tendency of malignant tertian parasites to agglutinate, so that "the infected red cells tend to become plugged in the capillaries of the viscera—brain, spleen, liver, intestinal mucous membrane, kidneys, lungs, bone-marrow—where they sporulate and cause local injuries and consequently symptoms referable to the respective viscera, the capillaries of which are plugged."[2]

Wherever parasites localise and sporulate, not only inflammatory conditions, but frequently destruction of tissue (molecular necrosis), results. Hence, in malignant tertian malaria, especially, we may have from brain lesions coma, delirium, convulsions, paralytic conditions, etc., from lesions of other organs

[1] BYAM and ARCHIBALD's *Practice of Medicine in the Tropics,* Vol. II, p. 580.
[2] E. R. STITT, *Diagnostics and Treatment of Tropical Diseases,* 5th Ed.

parasites into the surface blood by a mere redistribution, or by inducing vegetative reproduction. The author has no personal experience in the use of any of these methods.

Splenic puncture, with subsequent examination of the blood obtained in this way, helps diagnosis when parasites are absent from the peripheral blood, but it is not free from risk, and should only be adopted in very exceptional cases, as when it is necessary to diagnose between kala-azar and chronic malaria. In the former the microscopical field is seen to contain *Leishmania donovani* packed in splenic endothelial cells. Spleen puncture is decidedly not justifiable as a routine method of diagnosis in malaria. Results are not by any means always satisfactory as regards diagnosing the case. KNOWLES, ACTON and GUPTA,[1] in fifteen cases of malaria in which parasites were found in the cutaneous blood associated with enlarged hard spleens, adopted splenic puncture and "recovered few if any viable parasites, an occasional crescent, more frequently abundance of hæmozoin, and came to the conclusion that this procedure is of no diagnostic value in malaria."

There are many diseases from which malarial fevers have to be diagnosed. Among these the chief are—typhoid fever, paratyphoid fever A and B, pulmonary tuberculosis, pyæmia and septicæmia, tropical abscess of the liver, cerebral apoplexy, heatstroke, dysentery, pneumonia, relapsing fever, sand-fly fever, dengue, Malta fever, influenza, kala-azar (*quotidian* fever, anæmia, big spleen *and* liver, p. 204), ascariasis with pyrexia, acute rheumatism, hæmorrhagic pancreatitis, appendicitis, lymphangitis (especially with elephantiasis and filarial disease), anæmia, jaundice, "pyrexia of uncertain origin," and fever with gall-stones or inflamed gall-bladder. We can here only refer to the more common of these. The discovery of another kind of fever does not exclude malaria; malaria frequently complicates other fevers; it is very common with syphilis and pulmonary tuberculosis; indeed, it may be associated with any medical or surgical condition.

MALARIA IN RELATION TO OTHER INFECTIOUS DISEASES

Liability to secondary infections.—While what seems reasonable is not necessarily scientifically accurate, it would appear that an organism whose physiological resistance is considerably reduced, and whose blood-elaborating and eliminating organs are functionally defective (as is the case in malarial infection of any duration), is in a condition highly susceptible to secondary infections. Such infections are frequently associated with malaria.

Malaria and enteric fever.—These two conditions do not exclude one another. There are numerous districts, towns and cantonments in India where both are endemic, and cases are often seen in which the double infection has taken place. In rural endemic malarial districts enteric fever is rarely seen, and this may have something to do with the tradition, for a time current, that these diseases antagonised each other. Each form of infection is specific, and the one in no way prevents the other, as post-mortem records of large Indian hospitals show. Clinically, too, in many cases malaria parasites, the typhoid or the paratyphoid A or B bacilli, or the Widal reaction may be found in the same illness.

The writer's personal experience has been that usually the malarial paroxysms precede the enteric symptoms, the latter being to some extent masked by the dual infection, but sometimes the malaria is masked by the enteric symptoms; frequently the malaria parasites disappear from the blood for a time during the course of the enteric, and reappear during convalescence. Cases of enteric fever are recorded in which malarial paroxysms were made known by irregularities in the fever occurring periodically with marked anæmia. A positive diagnosis of either form of infection

[1] *Trop. Dis. Bull.*, Vol 20, December, 1923, p. 965, and *Ind. Med. Gaz.*, May, 1923, pp. 211–13.

February, his later attacks were about 11 a.m. every second day. In liver abscess, tuberculosis and pyogenic conditions the rise is usually in the afternoon or evening. The hectic fevers have a less definite division into cold, hot and sweating stages.

In a malarious place, during the malarial season, a quotidian fever (from mixed or double or triple infections) coming on before 11 a.m. is practically always malarial, before 12 noon very probably malarial, and before 1 p.m. probably malarial.

Of much help in diagnosis is the characteristic freedom from symptoms and almost complete return to comparative health the moment the attack is over. The patient may be pale and have a big spleen, but he does not complain of feeling ill. His appetite is good; he is not specially debilitated, he gains in weight and soon resumes his ordinary work. In relapse cases this often continues to be the life of the patient for months or years—relapses and rapid rallies contrast with the prolonged convalescence from enteric, dengue, influenza, sandfly fever, etc.

Study of patients' history.—In a person previously healthy and who is living in or has just left an endemic malarious place the sudden occurrence of a paroxysm is highly suggestive of malaria. Usually he will have had several similar attacks previously; his infection may have remained latent until a chill excites a paroxysm, such as occurs on reaching the hills from the plains in summer or autumn. *These remarks apply to all types of malarial fever.* A definite history of a cold, hot and sweating stage, followed by a return to good health, strongly favours the diagnosis of malaria.

Therapeutic quinine test.—It may be accepted as a rule that an intermittent fever which does not respond to daily doses of 30 grains of quinine for four days, provided that the drug is swallowed, absorbed and assimulated, as tested by the urine, is not malarial, although it may be malaria complicated with some other malady producing pyrexial phenomena. This, which is called the *therapeutic test* of malarial fever, is, next to the microscopic examination of the blood, the best diagnostic method we possess. This test should not be applied unless a microscopic examination cannot be made, for it is impossible to emphasise too forcibly the necessity of making certain, if possible, that the case is one of malarial fever before commencing to give quinine. If the case is not malaria, quinine is useless. If it is malaria, and quinine is given before the blood examination, the surface blood may be freed from parasites, and then the diagnosis may never be cleared up.

The work of J. G. Thomson seems to indicate that a complement-deviation test, using an emulsion of an organ rich in parasites as well as artificial cultures of the plasmodium as antigens, may be a help to diagnosis. (See Appendix VI—6.)

Provoking a relapse for diagnostic purposes.—The question of driving malaria parasites from their hiding-places in internal organs into the peripheral circulation for diagnostic purposes has received much consideration in late years, and many agencies have been employed for this purpose. The means used include—injections of sterile milk, sudden exposure to cold, solar irradiation, cold splenic douches, splenic massage, exhausting fatigue and violent exercise, X-rays or ultra-violet rays over the spleen, small provocative doses of salvarsan, subcutaneous injection of 2 to 3 mgm. of strychnine nitrate or 1 mgm. adrenalin. Reports seem to show that the last-named gives the largest proportion of positive results. It causes a very temporary reduction in the size of an acutely enlarged spleen, and parasites are shed into the peripheral blood within twenty minutes, but with the hard spleen of chronic malarial hypertrophy the results are not so marked. It is not known whether the provocative agents discharge the

T. recurrentis is found in the blood in large numbers during these attacks of fever moving about actively among the red cells, and there are no malaria parasites in these cells. Quinine has no effect on the disease; whereas salvarsan and its congeners act almost specifically. In the 1918 epidemic of relapsing fever in the United Provinces and Eastern Punjab there was a high percentage of cases of relapsing fever combined with malaria.

Cerebral apoplexy.—The diagnosis between the comatose form of cerebral pernicious attack and cerebral apoplexy, is often very difficult in the absence of an examination of the blood. In pernicious cerebral attacks there is usually a high temperature, and the spleen is enlarged. Cerebral apoplexy occurs in those of advanced years. An examination of the blood clears up any doubt.

Sunstroke.—Cerebral pernicious attacks may also simulate sunstroke, and it is well known that undue exposure to excessive solar heat predisposes to the occurrence of severe paroxysms in cases of malarial infection. The only way of settling the diagnosis is by examining the blood.

Pneumonia.—True pneumonia is diagnosed by the prolonged high temperature with no real remissions, the characteristic pulse-respiration ratio, the constant cough, difficulty of breathing and the expectoration having a "rusty" or reddish colour and containing pneumococci which give rise to the disease; there are no malaria parasites in the blood. Pneumonia, broncho-pneumonia or hypostatic congestion of the lungs may occur as a terminal incident in malignant tertian fever.

Malaria and syphilis.—Malaria and syphilis may not only occur in the same person, but the one disease considerably aggravates the other, and unless the malaria is promptly treated the dual infection is a very serious matter for the patient. During the years 1905 to 1909 the writer on three occasions obtained *Treponema pallidum* from the enlarged lymphatic glands of patients suffering from syphilis in whose blood malaria parasites were found at the same time.

Malaria and scurvy.—There are few of our Indian Frontier campaigns in which these two conditions are not met with in the same troops, the one aggravating the other. The scurvy comes on after some months' exposure to hardship and some physiological deficiency in the diet. This combination is common during famines and periods of scarcity, especially in the summer when green vegetables and fruit are limited.

Malaria and beri-beri.—The writer has been told by several practitioners of the Malay Straits, China and Formosa that they have seen both these conditions simultaneously in the same persons, but has no personal experience of this combination in India.

Precipitation of malarial paroxysms by surgical injuries.—Dormant malarial infection is sometimes awakened by accidental traumatic injury or even by the surgeon's knife in ordinary operations. Injuries of the spleen appear to be specially connected with arousing slumbering malaria, which has very strikingly followed splenectomies designed to eradicate the infection. During the Great War gunshot injuries often brought out dormant malaria. Parturition often arouses latent malaria.

Cases of malarial fever complicated with other diseases are more difficult to cure and more fatal than uncomplicated cases. There are districts in India, especially in Assam and Bengal, in which malaria is widely complicated with ankylostomiasis, and it is suggested that this concurrence is responsible for the comparatively small degree of success met with from anti-malarial measures.

Diagnosis of Fever of Unknown Origin.—It often happens that we are for a time quite unable to diagnose the true nature of a fever, and must set about doing so in a routine way. In the Army in India we have a very definite method of procedure in such cases. Say we have thoroughly examined the patient during the second day of the fever, which stands at 102° F. (38·9° C.), there is no enlargement of the spleen, no local organ is implicated in the disease, and up to the moment no malaria parasites have been found in the blood, although looked for in the ordinary way previously. The case is admitted and put on a milk diet, his temperature is taken every four hours; 5 c.c. of blood are

is very difficult to make upon clinical manifestations alone, and in dual infections such a diagnosis is quite impossible. Cases of severe malignant tertian with a continued or sub-continued temperature frequently run a course that closely resembles enteric; and the latter disease may often begin with a cold stage and intermittent rises of temperature and sweating, or have a remittent character, or assume this character from secondary infection during the later stages. In India this dual infection is well recognised clinically, and the original term applied to it by WOODWARD, *typho-malarial fever*, though scientifically inappropriate, is still used.

Malaria and tuberculosis.—It was at one time considered that malaria was antagonistic to tubercular infection in India. Ten years' practice in a large hospital has convinced the author that they aggravate one another. A frequent history in pulmonary tuberculosis is that it has been preceded by a series of malarial paroxysms or a number of relapses and rallies. Once the hectic stage is reached the tubercular factor dominates, and it is then rare (in this combined infection) to find malaria parasites in the blood.

Diagnosis of pulmonary tuberculosis from malaria.—In pulmonary tuberculosis there are practically always physical signs in the lungs to assist in the diagnosis. There are no malaria parasites in the blood. The tubercle bacillus is usually present in the expectoration after the first stage, and when present is readily found under the microscope after appropriate staining; quinine does not affect the course of the disease. Shivering or chills, fever and sweating, are usually of daily occurrence in the advanced stage of the disease, and the patient is usually greatly emaciated. The spleen is not enlarged as a rule.

Malaria and dysentery.—These two infections often occur in the same district endemically, and it by no means infrequently happens, especially in the later stages of malarial infection, that the two run their course concurrently in the same person. The paroxysms of malarial fever aggravate the dysenteric symptoms and the latter may then obscure the former. In such cases the detection of malaria parasites in the blood coincides either with a positive serum reaction to dysentery bacilli or with the presence in the fæces of *Entamœba histolytica*, according as to whether the dysentery is bacillary or amœbic. Moreover, dysenteric pernicious malarial attacks may simulate either bacillary or amœbic dysentery; hence in districts where malaria and dysentery occur the blood should be examined microscopically in every case of dysentery.

Malaria and tropical hepatic abscess.—In malarious districts, which are often also districts where amœbic dysentery is prevalent, tropical hepatic abscess and malaria are sometimes met with simultaneously in the same person. This form of abscess may show symptoms very similar to malarial fever; thus there may be shivering fits and fever occurring daily or irregularly, each bout of fever being accompanied by a cold, hot and sweating stage. With abscess of the liver, however, the diseased organ is usually enlarged, painful and tender, while the spleen is not enlarged, leucocytosis is marked, there is in a considerable proportion of the cases a history of antecedent dysentery, there are no malarial parasites in the blood, and quinine has no effect on the abscess. "At one time or another most liver abscesses are drenched with quinine on the supposition that the associated fever is malarial" (MANSON).

Malaria and septic infection.—Septic infection and malaria are frequently found together, in the same patient, both during malarious and non-malarious seasons, especially in chronic malaria and malarial cachexia. Pyæmia and septicæmia, and concealed collections of pus in the body, may be mistaken for malaria. In these conditions there are chills, fever and sweating, which usually recur *daily*, or come on irregularly, the chill, as a rule, beginning in the afternoon. There are no malarial parasites or pigmented cells in the blood, and quinine has no specific effect on the course of the disease.

Malaria and relapsing fever.—Malaria is occasionally found in association with relapsing fever, both malaria parasites and *Treponema recurrentis* being discovered in the blood of the same patient at the same time. Relapsing fever is diagnosed by the occurrence of *continuous fever lasting a week, then a non-febrile period followed* by another attack of fever similar to the first, but as a rule milder and shorter.

may be met with in simple quartan and tertian. These latter indeed may, if not properly treated by quinine, produce infections that last for years. Of the many complications of malarial fever the more serious are pneumonia, dysentery and diarrhœa, particularly when they complicate chronic malarial infection. In practically all cases the infection can be eradicated by the proper use of quinine. Hæmorrhagic cases (melæna, epistaxis, etc.) are sometimes alarming, and if not diagnosed and promptly treated, may prove fatal.

We have seen that the endemiology, epidemiology and symptomatology of malaria are highly complex, and it is obvious that they enter into the problems connected with prognosis. Unfortunately, as previously stated, we are still unacquainted with many factors entering into these complexities. It is necessary to bear in mind the definite distinction between malarial infection acquired during an epidemic period and that of the ordinary endemic season. This difference renders the question of grave importance as regards its probable severity, curability and prevention of relapses. Further, we have some definite knowledge as to the influence of quinine treatment in malaria. From a study of the mechanism of epidemic and endemic malaria we realise how unlikely it is that any two or three cases of malaria should be of the same severity or fatality, or should relapse with equal frequency, or should be modified or cured by the same course of quinine treatment, and we recognise the great importance of the source and origin of the disease.[1]

Epidemic malaria is an acute and often rapidly fatal disease. For the terrible effects of the 1908 epidemic in the Punjab see pp. 49, 50. Practically every one within its different foci was attacked seriously. An appalling number of pernicious cases occurred. The mortality was unprecedented, death being due in the vast majority of cases to the overwhelming intensity of the infection—a mortal malarial toxæmia. Therefore in the prognosis the questions of the source, time and place of the infection are most important.

Other factors are: age, sex, state of general health and constitution, presence or absence of concurrent disease, particular species of parasite and its numbers in the blood. As a general rule malaria is more serious in children than in adults, in women than in men, in the weakly than in the robust. It is specially serious in those debilitated from previous disease, badly nourished and in those unable to obtain or unwilling to take proper food. The lower classes are inclined to starve a fever, and consider the ordinary fever diet "heating" and will not take it.

Malaria is a very common cause of abortion among the masses in India.—It has been estimated by SUNDAR MOHAN DAS[2] that by abortion the potential population of Bengal is lowered by 800,000 annually, and it is judged by experience of 185 cases that 37·8 per cent. of these are caused by malaria. The child of the malarious mother, even if born at term, is liable to die within a few days, quite apart from the rare condition of congenital malaria.

Causes of death in acute malaria:[3]

1. Septicæmia—a massing of infected red cells in blood vessels of all vital organs	30 per cent.
2. Cerebral	50 per cent.
3. Cardiac	14 per cent.
4. Renal	1 per cent.
5. Suprarenal, pancreatic, rupture of spleen	remainder

[1] S. P. JAMES, "Malaria: Symptomatology," in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. II, p 1580.

[2] *Calcutta Med. Jl.*, 1923, reviewed by CLAYTON LANE in *Trop. Dis. Bull.*, Vol. 21, No. 4, p. 295.

[3] C. SEYFORTH, "Death in Malaria," *Trop. Dis. Bull.*, Vol. 22, January, 1925, p. 43.

abstracted *secundum artem*, 3 c.c. of which are added to an enteric-paratyphoid A and B medium and sent to the laboratory; a capsule of blood is taken for later serum reactions; a fresh preparation, a thin film and a thick film are made and examined for malaria parasites (see p. 142 *et seq.*). Usually the hospital diaphoretic mixture is given every three hours or so; if considered necessary an aperient is prescribed; *quinine is not given until malaria parasites are found in the blood.*[1] *It is decidedly wrong to give quinine before parasites are met with. There is no exception to this rule.* The films taken may show malaria parasites, *Spirochæta recurrentis*, *Microfilaria bancrofti*, etc., and suitable lines of treatment are then indicated. If no parasites are discovered we await the results of the blood culture and serum reactions. In enteric and the paratyphoids the diagnosis can be completed on the first or second day of the disease; if the blood has been taken within the first three days of the disease, and is negative, these diseases are absent. During this period the treatment is to be purely expectant, with nursing. We continue to examine the blood daily for malaria parasites, but no quinine is to be given until they are found. By the end of the third day, if malaria is present the temperature chart will show definite signs of intermittency, and probably also periodicity, or the chart may not help, but parasites are now found in the blood; in either case we begin quinine forthwith, and give sufficient doses. Suppose the temperature is quite indefinite or irregular, but in a few days tends to fall, and no malaria parasites are found, the case has to be returned as one of *pyrexia of uncertain origin*; in practice the name given to this class of case covers anything from the above to heatstroke, influenza, etc. If the fever continues high, say four or five days, and microscopic examination of the blood is still negative, the fever cannot be due to malaria, for no uncomplicated case of malaria lasts this length of time without remissions, and we also know that if there were sufficient parasites in the blood to create the pyrogenetic toxins to cause such fever, they would almost certainly be found in the peripheral blood, and as above stated, the chart would show intermittency and periodicity. If the fever goes on for a week and no diagnosis has been made, we test the serum again, this time also for Malta fever. If negative, and the temperature goes on or shows a tendency to a daily remission, we have to consider the possibility of three conditions—sepsis, hepatic abscess and pulmonary tuberculosis (p. 197). We carefully examine for all conditions of local sepsis—ear, throat, nose, pleura, pericardium, spleen, urine for indications of Bright's disease or sepsis in the urinary tract, fæces for *Entamœba histolytica*, ova of helminths, blood for streptococci in malignant endocarditis, leucocytosis, kala-azar (spleen puncture may be necessary), etc.; syphilis and all the diseases associated with splenomegaly, and cirrhosis of the liver.[2]

PROGNOSIS IN MALARIAL FEVERS

General remarks.—The prospects of recovery from malarial infection are usually good when the patient tolerates and can obtain proper quinine treatment and can be provided with an adequate quantity of suitable food, especially if he can be removed from the endemic area. Pernicious attacks are always dangerous, especially if of the cerebral or choleraic form, and more particularly in children and old people; they occur chiefly in malignant tertian infection, but

[1] The writer claims to have been the first to have introduced and insisted on the adoption of this rule in the Army in India. As previously stated, very exceptionally a case of cerebral pernicious malaria without parasites in the peripheral blood is met with: so seldom, however, that it should not affect the general rule laid down.

[2] For the above résumé the writer is greatly indebted to Lt.-Col. S. P. JAMES's "Malaria: Symptomatology," in BYAM and ARCHIBALD's *Practice of Medicine in the Tropics*, Vol. II, p. 1580.

malaria, since anæmia and œdema of the ankles are present in both; in ankylostomiasis there is no hypertrophy of the spleen, the characteristic ova of the parasite are to be found in the fæces if these are adequately examined, and disinfestation will produce improvement or cure.

Chronic malaria is gradually developed when the primary and succeeding infections have not been cured because enough quinine was not given over a sufficient length of time; or because the patient has some other complicating disease which in itself is lowering his resistance, and thus prevents his developing the defensive agencies that bring about immunity; or because he is the subject of malnutrition, due to food deficient in quantity, defective in quality or both. Unfortunately the last-mentioned factor is widespread among the masses in India. In chronic malaria all these conditions must be considered and dealt with if present. There is much destruction of hæmoglobin to be repaired, for which suitable drugs should be given, and quinine has to be administered over a long period—for three, preferably four, months. In relapsing cases a change of climate, especially to a cooler, non-malarious locality, sometimes acts like a charm.

Chronic malaria is a disease of complications. When it proves fatal, death is due to dysentery, broncho-pneumonia or some form of septic trouble, to which may or may not be added ankylostomiasis, tuberculosis, kala-azar, influenza, etc., whereas in acute malaria the chief cause of death is malarial toxæmia, with or without cerebral, cardiac, intestinal, pancreatic, suprarenal or hepatic involvement.

Malarial Cachexia

Malarial cachexia occurs in two fairly well defined forms—*acute* and *chronic*.

(*a*) **Acute primary malarial cachexia.**—Cases of this class have been again recognised. They were well known to physicians practising in India forty years ago. In endemic malarious districts we occasionally meet with acute primary malarial cachexia in the indigenous population. It is very common during epidemic malaria and not uncommon in areas of hyperendemicity in British troops, young British officers, European officials and tea-planters. The condition may, however, occur in anyone who has suffered from a series of severe malarial paroxysms, especially of the malignant tertian type if untreated.

The main symptoms are:—"Marked anæmia, great weakness, enlargement of the spleen and some emaciation. The tongue is coated; anorexia, nausea or even vomiting may persist; and there may be simple watery or bilious diarrhœa. The splenic enlargement may be considerable. The spleen is tender and easily ruptured. The liver is likewise usually enlarged. Albuminuria is nearly always present. There is marked depression; breathlessness, giddiness and palpitation on exertion. The arterial tension is very low, and various extra-cardiac bruits are heard on auscultation." The red cells are reduced to below 2,000,000, and in a few weeks may be as low as 1,000,000 per cubic mm. Malaria parasites are absent in some cases.

Hæmorrhages are common complications in malarial cachexia. The main forms are:—melæna, epistaxis, hæmaturia, hæmatemesis and (rarely) hæmoptysis. Epistaxis and melæna may be difficult to check. All these hæmorrhages are dangerous, some are fatal. In malarial cachexia surgical operations should not be undertaken without urgent necessity.

Anæmia and enlargement of the spleen.—The *anæmia* is directly due to the malaria; the erythrocytes are reduced to 2,000,000 per cubic mm. or fewer, and there is an *increase of the large mononuclears.* This latter with the

COMPLICATIONS AND SEQUELÆ OF MALARIAL FEVERS IN INDIA

CHRONIC MALARIA

Symptoms.—These cases are in a bad state of health; they suffer from bouts of malarial fever, have hypertrophy of the spleen which extends to the umbilicus or lower, are very anæmic, and have a general darkness of the skin with patches of melanosis on the face, buccal and other mucous membranes, but they are not emaciated, and during the apyrexial periods go about their work. They still suffer from what may correctly be called relapses and, during these, malaria parasites are found in the blood. They are greatly benefited by quinine. After reaching a certain stage they usually cease to get worse; even when untreated they tend gradually to get better, and if they can be removed from the risk of re-infection they recover. People suffering from chronic malaria or malarial cachexia may periodically get definite attacks of headache, neuralgia, neuritis, vomiting or gastralgia, or other clinical syndromes.

LIPKIN and RAMSDEN discovered that the quinine content of the blood in chronic malaria is lower than in healthy persons ingesting the same quantity. LIPKIN puts the alternative queries: Has the malaria become chronic because the quinine content of the blood has always been low, or has the content become low as the malaria became chronic? These questions remain unanswered.[1]

The clinical difference between chronic malaria and kala-azar is not always obvious. The following table gives the main clinical characteristics of each.

Chronic malaria.	*Kala-azar.*
Definite pyrexial and apyrexial periods of short duration. If a four-hourly temperature chart is carefully kept up and quinine treatment is withheld, the record will in the majority of cases present the *usual features of a malaria chart.* As in ordinary malaria, quinine checks the fever. Remember that parasites may be extremely difficult to find, especially during the rallies.	Fever present for long periods; its main feature is irregularity, intermittency is a secondary character; it is not affected by quinine.
Emaciation is exceptional; in the apyrexial periods the patient goes about and does his work. The splenomegaly is very pronounced; the hypertrophy of the liver, while present, is not a marked feature.	Progressive emaciation with weakness is a characteristic feature. The spleen *and* the liver are greatly enlarged. A spleen or liver puncture reveals the Leishman-Donovan body.

The whole question as to the difference between advanced kala-azar, chronic malaria and malarial cachexia is now well understood. Whilst chronic malaria is one of the most common conditions, real malarial cachexia is, at any rate, much less frequent. Although kala-azar is usually limited to certain localities, cases are met with occasionally in the most unlikely places.

Chronic malaria forms a large percentage of the cases met with when making malaria surveys in villages and towns in endemic malaria districts. It renders its victims particularly prone to other acute diseases, and to secondary infections such as amœbic or bacillary dysentery and pulmonary tuberculosis; and ordinary slight diseases and injuries may take on serious phases in which hæmorrhages are specially prone to occur. Sepsis in wounds or after surgical operations is predisposed to.

Ankylostomiasis has often been confused with the anæmia of chronic

[1] *Annals Trop. Med. and Paras.*, Vol. 12, p. 342.

The function of removal of the melanin falls chiefly on histiocytes (Kupffer's cells) of the liver and the histiocytic system generally, including the large mononuclears of the blood, but is also shared by the spleen, kidneys, lymph glands and mucous membranes of the intestines. So long as the bone-marrow and the organs named are capable of meeting the demands of the organism and of restoring the loss effected by the parasites, so long will there be no cachexia. When, however, anything interferes with the functional or structural integrity of these organs, then the clinical phenomena of malarial cachexia manifest themselves—in the case of functional disturbance the condition will be temporary, in the case of structural alterations, if these are at all serious, the condition will be permanent. In other words, when the tissues of the bone-marrow, spleen and liver become inefficient, then malarial cachexia develops. A vicious circle is set up. The hæmopoietic organs are called on for extra work, and being unable to receive adequate nutriment from the impoverished blood, fail to meet the demand upon them. In general terms it may be said that clinically this cachexia consists of symptoms connected with anæmia, hydræmia and lodgment of malarial pigment in the internal organs.

In developed cachexia the bone-marrow is yellow, sclerotic and gelatinous. Sometimes there is amyloid change in the kidneys with parenchymatous inflammation; more rarely there is amyloid change in the intestine, spleen and liver. Chronic malarial cachexia may lead to definite parenchymatous nephritis.

Malarial cachectics are in a high state of susceptibility to other infective and inflammatory diseases, from which they frequently suffer. Hence we should not attribute every morbid state observed to the influence of malarial infection in these cases.

Kala-azar

The association of the Leishman-Donovan body with a clinical condition very similar to that of malarial cachexia, has necessitated a closer investigation into the two groups of similar cases, and the outcome of observations during the last twenty-five years is the conclusion that a certain number of cases formerly called malarial cachexia and chronic malaria were in reality kala-azar.

Kala-azar is characterised by an irregular remittent fever, loss of body weight and emaciation, a peculiar cachexia associated with a darkening of the complexion, enlargement of the liver and spleen, often diarrhœa, sweating at night, well-marked secondary anæmia and progressive ill-health not amenable to quinine treatment. The average blood count may be stated to be about 2,400,000 red cells, 1,000 to 2,000 leucocytes—there is a relative increase of large mononuclears, but this is not constant; the hæmoglobin is greatly reduced. The parasite has been recovered from the peripheral circulation by examination of the blood by centrifugalisation; as also by puncturing either spleen or liver; abstraction of blood and cells from the latter organ is less dangerous than by puncture of the spleen. A full-sized hypodermic needle should be used and the strictest precautions adhered to (see p. 196). Quinine has no effect on the temperature of kala-azar. Apparent cures do sometimes occur spontaneously. The mortality, formerly about 90 per cent., has been greatly reduced by the use of tartar emetic intravenously. Kala-azar is not confined to certain parts of India; it has been seen sporadically in all parts of the country and in Burma. In its epidemic form it is now limited to Assam.

The parasite has been found in most organs, but is most numerous in liver and spleen. It is also found in bone-marrow, the lungs, testes, and ulcers of

splenic enlargement may be the only remaining specific indications of malaria. The spleen is sometimes very large, almost filling the abdominal cavity; usually extending nearly to the crest of the ilium below, half-way to the umbilicus in front—that is from 3 to 4 or 5 inches below the left costal arch. It is moderately firm on palpation and not painful. The capsule is thickened, especially its external surface, and there may be patches of adhesions from previous perisplenitis. Occasionally from great distension of its vascular sinuses one or more vessels give way, and fragments of spleen tissue may break up in this extravasated liquid blood.

All cases of malarial cachexia, acute or chronic, that are unable to quit the area of endemic malaria for a non-malarial one, run much risk; especially as they are very liable to other infections, which often take on an aggravated form.

(*b*) **Chronic malarial cachexia—clinical characters.**—Repeated frank attacks of malarial infection, improperly treated or not treated at all, are liable to culminate in the condition known as *chronic malarial cachexia*, the chief *symptoms* of which are anæmia and great enlargement of the splen. It occurs mostly in endemic malarial districts and especially follows malignant tertian, although it is by no means infrequent after neglected simple tertian and even after quartan malaria. It may exceptionally occur after latent and masked malarial infections that have gone untreated and unrecognised.

The associated symptoms are: gradually increasing weakness, dyspnœa, loss of appetite, and diarrhœa. There is no real emaciation such as is seen in kala-azar. There is much sensibility to cold, mental depression, defective memory and lack of power of concentration. There are periodical but irregular outbursts of malarial fever and during the intervals the temperature is normal. The parasites are found in the blood during these pyrexial attacks, but may completely disappear between them. There are long periods with normal or slightly subnormal temperature. Chronic malarial cachexia is often seen among children in endemic malarial districts. Of 3,884 children between 0 and 10 years of age examined in a large endemically malarious district, 2,330 or about 60 per cent. had varying degrees of enlargement of the spleen; amongst the splenic enlargements there were 98 cases, or 4·26 per cent., of malarial cachexia. The average malarial index of the 3,884 was about 40.

The skin.—The skin of the European suffering from chronic malarial cachexia acquires a peculiar yellowish or tawny hue, and the mucous membranes are pale. In natives the skin of the face becomes darker, with brownish or blackish patches. There is often œdema of the ankles and occasionally some ascites. The scleræ have a yellowish tinge.

The clinical picture of the fully developed disease, especially in children, is almost pathognomonic—large belly from enormous hypertrophy of the spleen, some enlargement of the liver and possibly ascites, attenuated legs, marked anæmia, unhealthy complexion with patches of pigmentation, rough, dry skin, melasma of the tongue and palate, marked anæmia, and œdema of the feet and ankles.

Pathology of chronic malarial cachexia.—In chronic malarial cachexia the pathological alterations are connected mainly with changes in certain organs, and, in this respect, are separated from the pathological effects of acute malarial infection, which are to a large extent confined to alterations in the blood. As we have seen in the early attacks of malaria, hundreds of millions of red blood corpuscles are destroyed by the parasite. This occurs also in every repeated attack. The restoration of the normal equilibrium in red cells has to be effected by the blood-forming organs. These same organs, at the time of malarial infection, remove the melanin and the débris of hæmoglobin set free during sporulation.

The parasites of malaria may during the attack be either scanty or absent, or there is an increase of large mononuclear cells. Roughly, blood examination on the first day shows parasites in 75 per cent. of the cases, on the second day 50 per cent., and on the third day 25 per cent. Malarial fever in India occasionally culminates in the production of blackwater fever, but this latter is not due to the direct effect of the malaria parasites in the blood at the time—the disease does not occur during the first attack of malaria in people recently arrived in India; in the endemic areas of blackwater fever it usually occurs after several paroxysms of malaria have been suffered from. One attack of the disease predisposes to another. Those who are attacked have in a large percentage of cases suffered from repeated attacks of malarial fever, although it very exceptionally happens that the first attack of blackwater fever occurs simultaneously with the first attack of malarial fever, especially when the person has lived in the endemic area for some time. Blackwater fever may be met with wherever severe malaria occurs, and it is not found where malaria is absent.

2. **That it is a form of quinine poisoning.**—This means that the symptoms develop after the administration of quinine. This is, however, only a determining cause in some cases, the condition of the blood previous to taking the quinine being such as to foster the splitting up of the red cells and solution of the hæmoglobin, which is discharged in the urine. The antecedent condition leading to this weakness of the red cells is believed by most authorities to be due to the effect of the toxins formed by the parasites of malaria. Blackwater fever may occur in persons who have never taken quinine.

3. **That it is a specific disease due to some undiscovered specific poison or germ.**—The evidence in favour of this view is in no way convincing. This theory has its origin in the analogy of the hæmoglobin in the urine to that of "red-water" or Texas cattle fever, which is due to a special protozoal parasite (*Piroplasma bigeminum*) in the red blood cells. No such parasite has been discovered in blackwater fever, and since the parasites named are microscopically gross bodies, and not minute or ultra-microscopical, such organisms, if present, would not have been overlooked by the many skilled observers who have investigated the disease in India and other tropical countries.

Course.—Following blackwater fever there is always serious anæmia and great debility; often also disturbances of the digestive system, and kidney disease. The essential factor in the disease is a destruction of the red cells, which is rapid and extreme; the hæmoglobin of the destroyed red cells is dissolved in the serum of the blood and thrown off by the kidneys. The amount of hæmoglobin in the plasma and in the urine is only a *small* part of the destruction—about one-tenth. The rest of the cells are probably digested by the histiocytes; anyhow, the rest of the hæmoglobin does not come into the circulation. Some of the hæmoglobin is taken up by the liver, spleen and kidneys and in course of time transformed into a yellow pigment (hæmosiderin). The skin and conjunctivæ become yellow, due to bilirubin in the plasma—presumably formed indirectly from hæmoglobin.

Diagnosis.—There is no disease met with in India for which blackwater fever can be mistaken. The reddish tinge of the froth on the urine after shaking is striking but not necessarily characteristic.

The special points about the diagnosis are—that in the vast majority of cases it occurs in a locality where the disease is endemic, the patient has usually suffered from one or more attacks of malarial fever previously, the disease sets in abruptly with a shivering fit followed by fever which may run high, the passage of blackish or brownish red urine, the occurrence of jaundice, severe and continuous bilious vomiting, the material having a bright green or olive

the intestines. There is a general blood infection, for PATTON has shown that the parasite of kala-azar may in a large percentage of cases be recovered from centrifugalised blood, by which process the leucocytes containing the parasite may readily be removed, stained and examined as ordinary smears.

Kala-azar appears to attach itself to houses, and may be considered a domestic disease, which favours the view that it is communicated to man through some insect. The Kala-azar Committee of the Medical Research Department in India have recently stated that the disease is carried from man to man through the sandfly *Phlebotomus argentipes*. *Leishmania donovani* has likewise been successfully inoculated into dogs in India and in Algiers. The evidence is rapidly growing that this parasite plays an important part in the fevers of India.

The parasites appear to be entirely intracellular in origin, and are found chiefly in the large mononuclear leucocytes on smears, and in the endothelial cells of the vessels of the liver and spleen *post mortem*. The parasites are very small but typical, from 1 to 2 μ in length, are round or oval, and possess a large and a small nucleus not unlike the micronucleus and macronucleus of a trypanosome. They have been cultivated *in vitro* in citrated blood by Sir LEONARD ROGERS, and develop into flagellated organisms which have most of the characters of *herpetomonads*.

BLACKWATER FEVER [1]

This is a very serious and often fatal fever occurring occasionally in the worst malarious places in India, and endemically in the Himalayan Terai, Assam, the Duars, certain parts of the East and West Coasts, and Burma. The disease is characterised by sudden onset, chills, irregular, intermittent or remittent fever, vomiting, difficulty of breathing, discharge of reddish urine (which becomes brownish and contains hæmoglobin), followed by jaundice.[2] It may attack all races in India, but long residence in an area where the disease is met with appears to give some degree of immunity. This is not invariably the case, as the writer has seen it in natives of Assam, the Garhwal and Kamoan Districts and Northern Burma, who had never left the area in which it was acquired. It is specially prone to attack Europeans in its endemic areas. The ultimate cause of the disease is still unknown.

Theories regarding the ætiology of blackwater fever.—There are various theories regarding its causation, of which the following three are the chief:

1. **Malarial origin.**—The disease is limited to areas in which malaria occurs not only endemically, but in its most severe form; during or preceding the attack malaria parasites are in the large majority of cases found in the blood, or there is a relative increase of the large mononuclear white cells as occurs in malaria, and in many instances these contain malarial pigment. As far as India is concerned blackwater fever is always preceded by or associated with malarial infection. "Blackwater fever is not a disease *per se*, but rather a condition of blood in which quinine, other drugs, cold or even exertion may produce a sudden destruction of red cells. The condition is produced only by malaria, and generally by repeated slight attacks, insufficiently combated by quinine" (J. W. W. STEPHENS).

Relapses are liable to occur, though usually of a less severe type than the first attack.

[1] From the writer's *Hygiene and Diseases of India*, 3rd Ed., pp. 590 *et seq.*

[2] But fever, hæmoglobinuria and even jaundice may be absent in blackwater fever; then the diagnosis is difficult.

diseases which most often mask the malarial infection. Occasionally in malaria surveys we come across acute apyretic larval infection. In masked infection we have one of several conditions which come on with *regular periodicity* and *disappear with quinine treatment*. The chief are—neuralgia, headache, chronic diarrhœa; but almost any form of disturbance of health may occur in this state.

Congenital Malaria

The occurrence of congenital malaria has long been doubted, but there are now cases on record which are certainly of this nature. Given favourable circumstances, infection of the fœtus through the maternal circulation does occur, possibly through rupture of some placental attachments. Malaria in the mother predisposes to accidents during pregnancy or at birth which may bring about direct infection of the infant. It is also recorded that infants are sometimes born with malarial infection, some enlargement of the spleen, parasites in the blood and paroxysms from the day of birth. In 1891 the writer attended a pregnant lady with benign tertian malaria in the seventh month. Under quinine treatment the malaria disappeared, but she gave birth to an infant with splenomegaly, who had regular benign tertian paroxysms for a month. That infant is now an officer in the Police Service in Burma. Damolard and Viallet reported a case in which a woman suffering from malaria gave birth to a child in which blood from the umbilical cord during life and from the heart after death contained malaria parasites identical with those in the maternal blood and placenta. A number of similar cases have been published, the most striking record being possibly the recognition of plasmodia from the blood of the prolapsed hand of an infant presenting transversely.

The protective action of the placenta both from maternal and fœtal points of view is shown by H. C. Clark.[1] It appears on the maternal side to be an optimum habitat for segmenting forms of *Plasmodium falciparum*, so that by its expulsion the mother is rid of numbers of them, while at the same time it rarely permits their passage to the fœtus, and then possibly only after traumatism. In malaria-infected women at parturition the placenta often prevents massive infection in the peripheral blood. All stages, including sporulating forms of the asexual parasite, are found. Incidentally, it may be remarked that in sub-tertian cases crescents are not found in the placenta. In malarial infection of the mother sections of the placenta show "enormous infection of the maternal sinuses, and a complete absence of this infection in the fœtal sinuses." H. C. Clark observed many malaria parasites in smears from the placenta taken at delivery, while the peripheral blood of the mother showed few or no parasites.

Blacklock and Gordon have shown that malaria in the mother, without infection of the child, causes a heavy infantile mortality within the first week of life. The fact that, with these massive placental infections, no "rings" are found suggests that possibly the parasites are dead.

Malarial marasmus.—Heavily infected bazaar or village children frequently die from a genuine *malarial marasmus*, or from some intercurrent disease, especially diarrhœa. Juvenile malaria may bring about stunted growth and retardation of puberty. Adults may suffer from a state of chronic malarial marasmus for years, during which time they usually suffer also from various intercurrent diseases.

Non-parasitic post-malarial fever.—The condition of *non-parasitic*

[1] *Trop. Dis. Bull.*, Vol 7, p. 15.

colour; the urine rapidly decreases in quantity and may finally be suppressed. It is probable that hæmaturia arising from other causes is sometimes called blackwater fever.

When the disease proves fatal death occurs early on the second or third day from the profound changes which occur in the blood, or in two or three weeks from the effects of suppression of urine, or some complication. (See Appendix VI—7.)

Latent and Masked (Larval) Malaria

(*a*) **Latent malarial infection.**—This signifies cases in which malaria parasites are to be found in the body, usually in small numbers, but occasionally in abundance, there being neither paroxysms nor any obvious signs of malarial infection. If not treated by quinine and not protected from mosquitoes these cases may act as "carriers" of malaria, although up to the present time there is no positive evidence to show that they are carriers.

The question of latency in malaria is one of profound interest: we are still only on the threshold of knowledge regarding it. Latency exists not only antecedent to relapses, but also to initial attacks. We produce thousands of cases of it in our troops in India yearly by the prophylactic use of quinine, the quinine possibly supplementing the action of anti-bodies in restraining the multiplication of the parasites and keeping them below the number required to produce actual malarial paroxysms. Latency may continue until something (pneumonia, operation, parturition) lowers the physiological resistance and permits malaria parasites to multiply in the blood.

When malarial fevers subside, either spontaneously or under quinine, the parasites as a rule vanish from the peripheral circulation. If quinine is not kept up this disappearance is only temporary. After some time, varying from weeks to months, the parasite reappears in the peripheral blood with the occurrence of a relapse of pyrexial phenomena. It selects certain organs or tissues in which to remain in a latent form. We do not as yet know whether the latent parasite has special characters, nor precisely the conditions which favour its multiplication and reappearance.

In latent malarial infection prior to clinical manifestations malaria plasmodia are going through their life-cycle in the spleen and can be demonstrated in sections of this organ after death. Were such latent infection suspected, malaria parasites might be found in aspirated splenic blood. Craig found that out of 1,267 cases of malaria, in which parasites were demonstrated in the peripheral blood, 395 or about 32 per cent. showed either "latent" or "masked infection." "As to the organ or tissue it selects, or as to its appearance and structure during this time of latency, or as to the exact conditions which cause it once more to resume active propagating circulating life, nothing is positively known."[1]

(*b*) **Masked or larval malarial infection.**—By this we mean a condition in which the symptoms of malarial infection are hidden by those of some associated disease, or in which the symptoms are so atypical as not to be recognised. Of the 395 cases mentioned above 275 were malignant tertian infections. Examinations of the blood in these cases showed the parasite in all stages of development, but always in small numbers. Of the 395 cases 277 were latent infections, that is, malaria parasites in the blood without symptoms, while 118 were masked infections, most of them being in patients suffering from diseases which masked the malarial symptoms. Chronic bacillary dysentery, amœbic dysentery, chronic diarrhœa and pulmonary tuberculosis are the

[1] Manson's *Tropical Diseases*, 6th Ed.

young broods of anophelines at the early stage of the rains begin afresh the process of universal infection of human beings. Hence we can readily see the very important rôle played by man in the perpetuation of malaria in India. There are probably thousands of millions of anophelines in every endemic malarial district; there are certainly thousands of them to every case of malarial infection. From this we can see how little is the effect of reducing anophelines, even if we could do so by one-half, so long as there are these millions of cases of untreated malaria for the other half to feed upon. Hence all malariologists in India insist that it is of more importance to endeavour to eliminate malaria by proper treatment than to endeavour to exterminate anophelines. Both tasks are at present equally impossible as far as India as a whole is concerned. It is not so in comparatively small districts, however, with isolated malarial foci, in which both measures—the universal employment of quinine in malarial infection and destruction of breeding-places within measurable distances of habitations—will go far towards reducing the endemicity. There are certain large districts also in which these measures may be employed with partial success.

Relapses occur after all forms of malarial infection, but are said to be much more common and persistent, and more obstinate to treatment in *P. vivax* infection. The author had the opportunity of inquiring into relapses occurring in several non-malarial places in troops returning from intensely malarious localities, especially in Lansdowne, Kohima, Almora and Dharmsala. Detachments sent to the Bhutan Frontier at the end of autumn annually from Shillong returned to a man with greatly enlarged spleens, anæmia and crescents in their blood. Amongst the 178 cases investigated there was not a single one of either benign tertian or quartan infection; in all there were relapses, and, during the relapses, only malignant tertian rings were found, and these were invariably followed by crescents. Again, during three years in Lansdowne the writer inquired into 161 cases of relapse and found crescents in 8 only, in one of which there was mixed infection with benign tertian parasites; the other 153 were all simple tertian. Of the 161 relapses, 130 were amongst Gurkhas (recruits and returned furlough men) who had passed through the Nepal Terai late in autumn and the beginning of winter, 30 were in Garhwali furlough men—two of the 8 malignant tertians were in the latter. In 1909 he ascertained that 35 per cent. of the relapses occurring in troops quartered in the Fort at Delhi, and 24 per cent. of those in Meerut, were due to *P. falciparum*, the remainder (except 1 per cent. mixed infections) were simple tertian infections.

When under skilled care and quinine treatment, benign tertian fever relapses from the fifth to the eighteenth day from the last paroxysm, malignant tertian in about a week, and quartan about the twentieth day. But there is no definite regularity in the time of the recurrence of relapses; they tend to become more and more remote from one another and the paroxysms to be of less severity. This is particularly the case in patients who are only partially treated by quinine after the attacks are over, as occurs in most hospitals. Relapses, when not properly treated, may continue for years.

The severity of the primary infections does not account for relapses; the mildest simple tertian and quartan may relapse persistently. Relapses are closely associated with conditions that lower resistance—exposure to chills, wetting, hot sun, alcoholic excesses, errors in diet, indigestion. Going to the hills from an endemic area on the plains, or the voyage to Europe from India, often starts a relapse. The acclimatisation of old European residents in India is really the experience and discretion taught by residence in the tropics.

There is still much in connexion with the life-history of malaria parasites with

post-malarial fever is a clinical entity in some of these cases. It is presumably unconnected with present malarial infection, for parasites are not found in the blood, and the condition is in no way affected by quinine. In many cases there is no discoverable complication. A number are probably due to pathological processes caused by the preceding malarial infection, such as fibrotic hyperplasia in the liver and spleen, necrotic processes from previous thrombosis, etc.

Relapses and Re-infections

Definitions of relapses, recurrences and re-infections.—By a *relapse* we mean the recurrence of a malarial paroxysm or series of paroxysms sometimes weeks, or even months, after an antecedent attack of malarial fever, without the intervention of a fresh infection—it is the reawakening of the clinical phenomena by malaria parasites that have remained dormant in the body from a previous period, a renewed activity of quiescent parasites. They are unconnected with re-infections. Some authorities write of relapses under two headings: a *true relapse* occurring after a short interval from the preceding paroxysms, and a *recurrence* after a much longer interval. A *parasitic relapse*, which may be febrile or afebrile, signifies that parasites have reappeared in the blood after having temporarily vanished under treatment. By *re-infection* we mean a new infection of the blood by malaria parasites through infected anophelines, after the system has, by treatment or spontaneously, got rid of all parasites by which it was previously invaded.

In a malarious district during the malarial season, when fresh infections are constantly liable to occur, it is practically impossible to decide whether a particular case is one of re-infection or relapse except in the case of non-immune immigrants shortly after arrival. Many of the so-called relapses are re-infections. This is a fact often lost sight of. Re-infection is very common during the malarial season when infected man and infected anophelines coexist. A careful anamnesis of each case, with examination of the blood, and a history (if any) of the course of the infection, would probably give us information upon which we could draw inferences as to whether it was a re-infection or a relapse, but such deductions would not be scientifically reliable (see p. 174). The only positive indication of a re-infection would be a record to the effect that the preceding attack was caused by a species of parasite different from the one discovered in the blood during the attack under investigation. But even then, it might be, and every now and again is, a mixed infection with predominance of one species of parasite at a time. Relapses are evident also when malarial paroxysms occur in a non-malarial locality in a person who has recently left a malarial place, in which latter he had suffered from malarial fever. Re-infection from members of the family or persons occupying the same building is a frequent cause of supposed relapse. In such cases the whole family or occupants of the building should be examined for malaria and any discovered carriers treated.

Relapses must in India be looked upon as ordinary sequences of malarial infection; they are the rule and not the exception; they occur in over 90 per cent. of cases not properly treated by quinine. For the eight millions of cases that are brought under treatment in hospitals, jails, asylums, and among the men of the Army in India, there are a hundred million cases that are never recorded and comparatively few of them ever get quinine. These occur chiefly amongst the impoverished labourers and ryots, whose condition of nutrition and lowered resistance renders them specially prone to relapses. It is the cases of relapse occurring during non-malarial seasons that serve to maintain the breed of malaria parasites throughout the year; from them the

14

C. F. CRAIG,[1] MANNABERG [2] and others believe that as the result of the conjugation of two young schizonts a more resisting parasite is formed, which, in conditions favourable for development, may begin a fresh asexual cycle. SCHAUDINN considered that, either spontaneously or as the result of treatment, asexual forms and male gametes disappeared, females surviving and eventually, through the process of parthenogenesis (p. 218), producing merozoites which set up an asexual cycle.

Sir RONALD ROSS believes that the asexual parasites breed during the rallies just as they do during the relapses, except that during the rallies they are not produced in sufficient numbers to cause paroxysms. In a special investigation Sir RONALD ROSS and D. THOMSON found that the parasites are present in the intervals between the relapses and multiply considerably during the relapses. They demonstrated that the number of parasites required to produce a paroxysm was roughly 250,000,000 in an average man, but during a rally the numbers fall to a few per cubic centimetre, while during a relapse the numbers may reach a total of many thousands of millions, even more than one million millions. This suggested the necessity of giving quinine over a long period until every parasite is extirpated. The writer advocated this measure in 1909 [3] and reproduced his views in *Prophylaxis of Malaria in India* in 1910. BIGNAMI holds with Sir RONALD ROSS.

There are exceptions to the general rule in that the cutaneous blood is not a sure index of the presence of malaria parasites in the body, for we may, of course, have a paroxysm with "no parasites" in the peripheral blood and the reverse—abundant parasites without paroxysms.

A great deal has been written about the ease with which a short course of quinine (total 90 grains only) cures malaria induced by injecting benign tertian blood into general paralytics, and comparisons have been drawn between this and the difficulty experienced in effecting cures in this form of infection acquired in the natural way in endemic malarious places. When infection of general paralytics is induced by mosquito bite a high proportion relapses. Nevertheless, the infection in the latter case disappears, either spontaneously, or, if not, after a few, generally after a single repetition of this short course.[4] The two groups of cases—naturally acquired and induced malaria—are not comparable. There is one specially noteworthy difference in the ordinary cases of benign tertian acquired in India, and cases of mosquito-induced malaria in general paralysis in Europe. In the former the victims are probably bitten by many infected Anopheles on several occasions and several re-infections are superimposed on the primary one; in the latter, infection is induced by the bites of five to ten infected Anopheles on one occasion only. The explanation appears to be that in these induced cases *primary malaria* is treated early and properly by quinine; the majority of the cases in endemic malarious places are old-standing relapse cases or chronic malaria.

Work in connexion with the problem of the cause of relapses is still in progress in many parts of the world, and it would be premature to make further statements regarding the results except that certain undescribed parasitic forms are said to be found in the blood of relapse cases of benign tertian, mostly intracellular (Plate XI, Figs. 54–57). It is possible that these represent forms

[1] *Malarial Fevers*, p. 244.

[2] "Malarial Diseases," in Nothnagel's *Encyclop. of Practical Med.*, English Translation, pp. 71, 72.

[3] *Malaria Report of the 7th (Meerut) Div.*, 1909, App. II, p. 81.

[4] WARRINGTON YORKE, *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XIX, No. 3, p. 109 *et seq.*

which we are unacquainted, and one of the most difficult problems is the exact pathogenetic relations of relapses. We have been accustomed to believe that malaria parasites, like all other sporozoa, after several generations of asexual life, tend to exhaust themselves, but the recurrence of malarial fever for years in persons who have left the malarious locality in which they acquired malarial infection, and lived in non-malarious places, that is, without the possibility of re-infection, indicates that such asexual multiplication may continue almost indefinitely. In Lansdowne (5,600 feet), where there is no initial malaria, the writer has seen cases of such relapses going on for at least three years. There is undoubted evidence that such relapses may go on for a much longer period. Dr. ANTON BREINL, formerly of the Liverpool School of Tropical Medicine, demonstrated malaria parasites in the blood of a patient who had not been in any malarious place *for seven years*. CASTELLANI states: "I have seen cases having relapses in England for seven or eight years after leaving the Balkans."[1] There is probably much more in relapses than is accounted for on the simple explanation of parthenogenesis and a return of female gametes to "indifferent" forms. A special form of the parasite has been incriminated in relapses.

The clinical characters of chronic malaria and repeated relapse cases are very different from those of acute primary malaria. In the former groups the patients are always anæmic; the red cells are greatly reduced in number, and the hæmoglobin in the remaining cells is from 10 to 50 per cent. below normal; the blood-forming organs are functioning defectively; the spleen is enlarged, the action of the liver and kidneys is interfered with, and sometimes pathological changes have occurred in these organs. The resistance is therefore greatly lowered, and in many cases some other disease complicates the malaria and still further lowers vitality. The malaria in such cases is rarely eradicated by quinine alone. All experienced practitioners in India know how slight is the influence of quinine in the cachexia developed from lasting malaria without using building-up and tonic treatment simultaneously. Experience of debilitated troops during the Great War emphasised this point; good, wholesome fresh food and good climate had a great deal to do in curing those weakened by malaria.

It would appear that for a time at least after the original attack the susceptibility to re-infection is increased, although after a series of re-infections this susceptibility seems to be lessened. The re-infection may be by the same species of parasite as in the former attacks, or by another species, showing that the individual species brings about no immunity against re-infection.

The strain of the parasite has probably nothing to do with relapses. During the war malarial patients from such widely different places as Macedonia, East and West Africa, Mesopotamia, and the North-West Frontier of India all relapsed to about the same extent.

In endemic malarial places those infected with malaria suffer from repeated groups of paroxysms—sometimes one after another in quick succession. If these cases are sent to non-malarious hill stations or comparatively healthy plains stations, the interval between each series of paroxysms at once lengthens. This is so marked that it would be unreasonable to attribute it to improved health effecting a sudden decrease in the number of parasites harboured by the patient, and rational to believe it to be due to cessation of re-infections.

As has been noted, our knowledge of the life-history of the parasite in the intervals between groups of paroxysms (without re-infection) is at present far from complete. The explanation of relapses is to a large extent based on hypotheses, which may or may not eventually be proved to be sound and reliable. Among the theories put forward the following are the more important.

[1] *International Conference on Health Problems in Tropical America*, 1924, p. 73.

sary in the system of nature, and the male is taking on the pangs of labour. The author is not disposed to dogmatise upon this question, which is still *sub judice.*

SPONTANEOUS CURE OF MALARIA

It is within the experience of all medical men in India that in healthy persons an attack of malaria may be slight and completely thrown off. In all probability a similar infection, when the physiological resistance is reduced from any cause, would bring about definite symptoms of malarial infection. At Lansdowne (5,600 feet), where no fresh infection arises, the author has frequently tested this. Even pernicious cases may recover spontaneously: "several such cases have been reported by TORTI."

In investigating the malaria of the 7th (Meerut) Division in 1909 the writer made the following observation, which he believes is unique of its kind. "Of 987 native children examined on hill stations (height 5,000 to 7,400 feet), in which no initial malaria existed, I found that there were 101 or about 10 per cent. with enlargement of the spleen. They had all been resident on the hills for from ten to twelve months; before that they were in endemic malarious stations. None of these children had been under quinine treatment. They were the children of native followers of European troops quartered in hill stations. In 3,884 children under ten years of age in the plains the spleen rate was 60 per cent., in the 987 children in the hills 10 per cent., therefore 50 per cent. of the splenic enlargements (in the absence of re-infections) disappeared spontaneously within twelve months. The endemic index in the 3,884 children was about 40 per cent., that of the hills children 5 per cent." [1]

The human body possesses some natural means of destroying the malaria parasite. One agency by which this is brought about is the large mononuclear leucocytes, and to a less extent the polymorphonuclears, possibly also splenic endothelial cells. The leucocytes effect the destruction of some of the parasites during the febrile paroxysm, and also ingest the disintegrated forms after the conclusion of the febrile attacks. There are, in all probability, other undetermined factors in operation in bringing about spontaneous cure. When the nutrition of the body is perfect this and other defensive natural processes are considerably helped, whereas when the vitality is lowered from any cause spontaneous cure is hindered; but the essential mechanism by which spontaneous cure is effected is a subject regarding which our knowledge is still very incomplete; it calls for special investigation. ACTON,[2] in 1919, advanced the view that natural cure results from the exhaustion of the asexual cycle by its conversion into gametocytes, which are destroyed by phagocytes or die of senility.

The mechanisms of natural and artificial cure are considered by some to be quite different. Many are of opinion that quinine does not aid the natural process of cure, and, indeed, may even retard it. Others believe that quinine cures by abrogating the asexual cycle of the parasite, an eventuality which is considered not to occur naturally. A large number of workers have pinned their faith to the view that sterilisation is at least in part brought about by the formation of anti-bodies of some kind, and this is now the view that the writer holds.

MACFIE and WARRINGTON YORKE [3] have advanced the following hypothesis regarding the mechanism of cure of malarial infection under quinine treatment:

[1] *Report on Malaria Survey of the 7th (Meerut) Division* (1909), App. II, p. 107.

[2] *Trop. Dis. Bull.*, Vol. 18, p. 335.

[3] "Observations on Malaria made during Treatment of General Paralysis," *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XVIII, Nos 1 and 2, p. 13.

of the parasite developed against the resistance of the patient in chronic infections. S. P. JAMES (1917) suggested that persistent or latent forms which have hitherto escaped recognition because of their general resemblance to gametocytes may be the cause of genuine relapses as distinct from recrudescences.

Parthenogenesis.[1]—Regarding many of the points mentioned we find analogies in the process of development of sporozoites in *Eimeria*, whilst as regards relapses it has been said by some authorities that gametes, which do not leave the blood, collect in internal organs and subsequently, as "*indifferent*" parasites, are capable of taking up the process of schizogony, resulting in the invasion of red blood corpuscles by the spores so formed.

SCHAUDINN considered that certain findings of his indicated the occurrence of parthenogenesis in the malaria parasite. J. D. THOMSON has shown that the findings mentioned represent two schizonts, both possibly segmenting, infecting the same red cell. Combined infections of schizont and male or female gametocyte or even two gametocytes in one cell are occasionally met with (Fig. 71).

Lt.-Col. A. ALCOCK, C.I.E., F.R.S.,[2] states: "In postulating the reversion of a gamete into a schizont—the gamete always being a particularly determined and highly differentiated cell—SCHAUDINN invoked a phenomenon which, so far as is known, is unparalleled in biology." Again he writes: "As parthenogenesis can only imply that a virgin ovum completes a predetermined course of evolution, exactly as if it were a fertilised ovum, the progeny of a plasmodium macrogamete must, under any supposed circumstances, be a swarm of *sporozoites, not a mass of trophozoites*."[3]

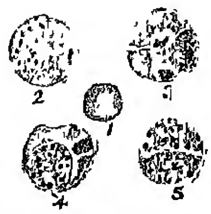


FIG. 71.—Abnormal malaria parasites. 1, Normal red cell; 2, gametocyte and schizont; 3, gametocyte and gametocyte. 4, gametocyte and schizont, 5, schizont and schizont, both undergoing schizogony.

From MANSON'S *Tropical Diseases*, 8th Ed., after Dr. J. D. THOMSON.

Lt.-Col. C. M. WENYON[4] expresses an equally emphatic opinion against the theory of parthenogenesis.

We cannot, however, ignore the fact that parthenogenesis of malaria parasites is supported by *some of the greatest living malariologists. The Bulletin de la Société de Pathologie Exotique*, March 8, 1922, *contains the Rapport de la Commission du Paludisme.* Commission désignée à la séance de Novembre et composée de MM. MARCHOUX, Président, G. MARTIN, ROUBAUD, Membres, ED. SERGENT et J. RIEUX, rapporteurs. This important Commission stated definitely: "Mature gametes remain permanently enclosed in erythrocytes deprived of their hæmoglobin. These are not immortal; *a certain number regenerate by parthenogenetic division into schizonts.*" LAVERAN also held this view, as did GRASSI.

This, after all, is an opinion based on the interpretation that certain forms seen are macrogametes producing schizonts and not a macrogamete and a schizont parasitising the same cell, whose outlines are indistinguishable. If this interpretation be accepted, then there must equally be accepted the interpretation that a microgamete can reproduce by parthenogenesis, for IOFF has shown that the appearances are exactly similar. The female becomes unneces-

[1] *Parthenogenesis* simply means asexual or virginal reproduction. The word "*indifferent*" is applied here to parasites that may develop into asexual or sexual forms.

[2] *Trop. Dis. Bull.*, 1918, Vol. 11, p. 1, abstracting J. D. THOMSON.

[3] *Ibid.*, 1922, p. 274, abstracting J. D. THOMSON.

[4] *Jl. R A.M.C.*, 1921, Vol. 37.

B.—CLINICAL PATHOLOGY OF MALARIA

In this section an effort is made to give the pathological processes and morbid changes with which each symptom in malarial fevers is associated, and to attach to each its significance so far as we are acquainted with it. Many of the symptoms occurring in paroxysms of malaria may now be explained, and to a certain extent correlated to the life-history of the parasite in the body. There are, however, still many gaps in our knowledge. We can connect the different stages of an attack with definite changes in the blood and tissues, but can only speculate as to the actual pathological process to which some of the symptoms are due, *e.g.* how the toxins give rise to pyrexial phenomena, why an intense parasitic invasion is followed by persistent low blood pressure, why the parasite in perniciousness concentrates its harmful effects in one case on the cerebrum, in another on the intestines, in others on the heart, pancreas and suprarenal glands.

It is proposed to deal with the pathological significance of symptoms in the following order: Early Effects of Malarial Infection; Habitats of Malaria Parasites in Man; Effects of Simultaneous Sporulation of Parasites; The Fever; Blood Changes, Anæmia; The Leucocytes; Other Cells; Phagocytosis; Hæmozoin; Post-Malarial Anæmia; Enlargement of the Spleen; Digestive System; Enlargement of the Liver; Nervous System, Circulatory System, Skin, Respiratory System, Urinary System, Muscular System and Suprarenal Glands in Malaria.

Early effects of malarial infection.—At the moment when the proboscis of a malaria-infected anopheline is inserted into the skin, sporozoites are injected into the blood. It is still doubtful as to how many ordinarily get into the blood with each bite. We may reasonably assume that if the bite is very momentary only comparatively few, if any, will reach the blood. But an infected mosquito inside a mosquito net will be injecting sporozoites each time it sucks up blood. The bite of a single mosquito is certainly sufficient to cause malarial infection. Judging from the thousands of sporozoites that are seen in the salivary glands and body cavity of infected mosquitoes on dissection, a very considerable number must be injected at each bite.

Suppose that 1,000 sporozoites find their way to the blood stream. For the moment 1,000 are of no consequence. This leads one to ask the question as to what number of injected sporozoites are required to produce malarial fever, and the percentage of infected red blood cells that produce malarial pyrexial phenomena. Ross answers these questions by stating that the red cells in man may roughly be computed as 25,000,000,000. Assuming that 1,000 sporozoites enter the circulation. Each segmenting quartan parasite at the end of 72 hours gives rise on an average to 6 to 10 spores, each benign tertian parasite 12 to 24 at the end of 48 hours, and malignant tertian from 10 to 27 in the same period. Much of this is highly theoretical, as there is little or no evidence to support it; indeed, the writer is disposed to consider it, to say the least, rather doubtful.

Ross and Thomson (1910) found that 200 to 500 *P. vivax* and 600 to 1,500 *P. falciparum* per cubic mm. are required to cause a malarial attack. In a case of simple tertian malaria in 1909 the writer found 15·5 per cent. of the red cells infected. The particulars of the case are given later on. Much heavier infections in malignant tertian are not uncommon, especially during epidemic malaria. An infection of 1 in 100,000 red cells is probably the lowest capable of producing pyrexial phenomena in a fresh infection.[1]

[1] It should be remembered that the peripheral blood and the whole blood of the body are very different things.

"*Quinine given to a patient whose blood contains numerous malaria parasites invariably destroys directly, or more probably indirectly, large numbers, but not all, of the parasites, thus setting free a considerable quantity of soluble antigen. The antigen promotes by stimulation of the host's tissues the formation of immune-body. The immune-body, if present in sufficient amount, destroys the remaining parasites, thus resulting in sterilisation of the infection and in the cure of the patient.* As will be seen, this hypothesis embodies two postulates · firstly, that no form of quinine therapy *per se* ever destroys all the malaria parasites in the human body, and secondly, that the tissues of the host are able, in response to antigen stimulus, to produce a sufficient quantity of immune-body." But if quinine is necessary to set free soluble antigen, which stimulates the tissues to produce immune-body, why should the immune-body kill the parasite which has *ex hypothesi* no free antigen?

In India there are millions of cases of malaria yearly who get clinically well without taking, or having an opportunity of taking, quinine. It is obvious that there is some natural curative agency by which such recovery is brought about. "It is when we consider malaria as an infection of the human host by a parasite, which in the majority of infections lasts for at least three or four months, and in exceptional cases for years; in which the relationship of the parasite to its host is that of enemies at constant war; where for a time first one and then the other may be in the ascendant; and where victory in the end may be to either, that we can understand the apparently contradictory results of quinine."[1]

When the vitality is from any cause lowered the asexual parasites multiply and are found in the cutaneous circulation. The contest continues, and when the life of the parasite is menaced, the asexual proceed to develop into sexual forms, which are responsible for the perpetuation of the species. At this particular stage the human host becomes a danger to those about him, if anopheline carriers of malaria are present. But gametocytes may be among the first forms discoverable in the circulating blood. It has to be confessed that much of this reasoning is hypothetical. A good deal of our difficulty in malaria arises from our not being able to examine the organs constantly to see what is really going on. It is highly probable that study of chimpanzee malaria of West Africa may clear up several points that are obscure.

If the health and vitality of the human host are improved the parasites decrease, may vanish from the surface blood, may die or be destroyed by the host. If enough quinine is given the human host gradually overcomes the parasites, and in doing so may be but little affected by them; but he is for part of this time at least instrumental in infecting others—he is a malaria-carrier.

The question arises as to whether two separate immunities are acquired to bring about the destruction of the parasite. "It appears to me to be not uncommon for the host to become immune to the poison causing the toxin long before it acquires power to reduce the number of parasites; for cases with numerous parasites and without pyrexia over considerable periods are not uncommon, indeed are recorded by every writer on malaria."[2]

Without quinine many cases of malaria, especially in highly endemic places, would die before they could acquire the resistant power necessary to destroy the parasite. It is possible that the real effect of quinine is to help man to bring about in some way for himself the power to free himself from the disease.

[1] Sir MALCOLM WATSON, *Prevention of Malaria in the Federated Malay States*, 2nd Ed., p. 114.

[2] *Ibid.*, p. 115.

The fever.—The fever in an ordinary typical malarial attack is very definite and characterised by intermittency and periodicity (p. 194). The fever ceases at intervals—is intermittent; it alternately falls to normal (in fact, usually well below normal) and rises again. This is so well marked in benign tertian and quartan infections that they have long been called *the intermittent fevers.*[1] Periodicity refers to the recurrence of malarial fever at regular intervals of time. Microscopic examination of the peripheral blood shows that the intermittent and periodic fever coincides with particular stages in the growth and multiplication of malaria parasites in the surface blood and internal organs (p. 180). The schizonts grow until they reach maturity, then the red cells burst, set free the spores and toxins into the plasma, and the spores are once more ready to invade other red cells. At the time that the parasite is approaching its full size there is neither fever nor other symptoms, but as soon as some of the parasites are set free from the red cells the paroxysm begins. In quartan malaria, sporulation can be seen in the peripheral blood a short time before the cold stage, and it may be observed that before the hot stage ends there are many fresh quartan rings in the red cells.

While growing in or on the red cell the parasite is feeding on the hæmoglobin and creating a pyrogenetic toxin, but this remains there until it is set free into the plasma, when it acts on the pyrogenetic centre of the nervous system and causes the temperature to rise. It will be recognised that with the various forms of mixed infections (p. 180) we may have much variation in the febrile attacks and in the curves of the temperature charts. We may even have overlapping of the paroxysms, when the fever may be remittent or continuous. Even with a single infection of one form of parasite the temperature may be atypical. For example, the day of the paroxysm suddenly changes without any obvious cause. This is seen in one or more cases in every large malaria ward of hospitals. It is sometimes a conspicuous feature in the induced benign tertian malaria for the cure of general paralysis. Again, anticipation or postponement may occur (p. 178)[2]; or, in malignant tertian, some groups of the parasite of the same brood sporulate at different times of the day and may give rise to a prolonged hot stage. Further, the whole range of the temperature chart may be altered by the improper use of quinine (p. 183). If quinine is given in too small doses, or irregularly, or by the mouth when there is much disturbance of the digestive system, the temperature may be kept continuously high. It has been stated, the writer believes wrongly, that these latter are cases of "quinine fever" (p. 266). When in such cases care is taken to ensure that the drug is properly absorbed it will be found that most of them can be more correctly classed as "quinine-resisting fever." With this remark, quoted from Lt.-Col. S. P. JAMES,[3] the writer is in full agreement. In early untreated relapses we can, as a rule, correlate the life-cycle of the parasite in the blood with the various stages of the paroxysm, but in the later relapses, frequently this cannot be done, for then we often get cases with no asexual parasites (or these are so few as to be found with difficulty) and yet with regular paroxysms; these are the so-called *paradoxical relapses.* In some of these cases we come across crowds of crescents, which appear to be shed into the peripheral blood periodically. Or we meet with *parasitic relapses,* with numerous asexual parasites in the surface blood without any symptoms, a group of cases called *apparently healthy malaria-carriers* (p. 54). These divergences indicate that

[1] See the earlier editions of the *Nomenclature, Royal College of Physicians of London.*

[2] Anticipation is quite a feature of many induced malarias for general paralysis.

[3] Article, "Malaria Pathology," in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics,* Vol. II, p. 1571.

Habitats of malaria parasites in man.—BLACKLOCK [1] suggests that the optimum habitats of the sexual and asexual forms differ, that for the gametocyte being the bone-marrow, and that for the segmenting forms the spleen. W. M. JAMES [2] considers the optimum habitat of crescents to be the rib marrow (see section on PARASITES OF MALARIA). "*Much of the* existing diagnostic confusion results from the belief that the optimum habitat is the blood" (CLAYTON LANE). It may not be in the circulation at all in certain circumstances.

Vast numbers of parasites may exist in the body for long periods without producing paroxysms in those who are approaching completion of their toleration. The writer has notes of a native boy of twelve years in Bareilly, in 1909, who had had no appreciable fever for several months, but had a greatly enlarged spleen. On August 20 the fields of stained smears contained 2 per cent. of erythrocytes infected with benign tertian schizonts in various stages of development. This percentage continued for a whole week, the blood being examined daily. At the end of this time the number gradually increased until an average of 5·8 per cent. was reached, and the writer hazarded the prediction that a paroxysm was impending. A frank paroxysm occurred on the forenoon of September 2. Similar cases of latent chronic malaria are common among children over five years of age in all endemic areas.

Effects of simultaneous sporulation of parasites.—The time of commencement of the paroxysm coincides with that of sporulation of the parasites in the blood. This simple biological observation by GOLGI has swept away volumes of unfounded theory. The coincidence is nevertheless relative; there is, as a rule, a difference of several hours between the ages of the parasites seen on every slide, even in those of quartan, in which we have the nearest approach to simultaneous sporulation. In *P. falciparum* infection a close examination of any slide shows that it holds very young unpigmented amœboid parasites resting on the red cells, and fully formed rings and egg-shaped forms within the red cells, the last-named being the highest stage of the evolution of the parasite ordinarily seen in the peripheral blood.

That toxic bodies are set free at the moment of bursting of the red cells and liberating of the merozoites is extremely probable. The toxicity of the urine after a paroxysm is higher than normal, although the experiments hitherto conducted to prove this must be accepted with some reservation. It is assumed that the toxins give rise to the paroxysms by their effects on the vaso-motor centres and thermotaxic mechanism. They are comparable in this respect to the toxins manufactured by bacteria in septic and pyæmic states; indeed, in the latter we have as yet no adequate explanation for the periodical return of fever, etc., whereas in malarial fever such an explanation is presented in the biological evolution of the parasite with each paroxysm of fever. We are aware that some high authorities refer the periodicity of the paroxysms to an intermittent activity of the phagocytes; and that in order to explain the various types of fever they presuppose a greater or less activity on the part of the parasites in different countries, together with a difference in the reaction of the human organism. The known biological facts in regard to the parasites are, however, so intimately connected with the clinical phenomena of a paroxysm, that one feels forced to accept the view originally propounded by Golgi—that the paroxysm is due to the sporulation of the parasites more or less simultaneously.

[1] "Notes on a Case of Indigenous Infection with *P. falciparum*," *Ann. Trop. Med. and Parasit.*, April 27, 1921, pp. 59–72

[2] *Intern. Conf. on Health Problems in Trop. Amer.*, 1924, pp. 67–69.

the red cells were only 500,000 (KELSCH). A degree of anæmia which reduces the red blood cells 20 per cent. after the first few paroxysms is common. The anæmia, however, is not progressive, although the effects may be somewhat lasting. After prolonged, severe infections there is often a reduction of even 50 per cent. of the red cells, and about the same percentage loss of hæmoglobin. Here, again, some at least of the estimates regarding cell volume and numbers are highly theoretical, and the writer does not rely upon them. We know, for example, that as regards cell volume the *normal* varies from 36 to 52 per cent.

From the above statements we can readily explain the *anæmia*. Its degree depends on the number of red cells infected by parasites, the speed with which these parasites multiply, and the extent to which uninfected cells are hæmolysed; it is also to some extent dependent on the degree to which the malarial process affects the functions of the blood-elaborating organs. The blood cells are not replaced as rapidly as destroyed, hence there is (within certain limits) after each series of paroxysms a greater degree of anæmia. After mild infections the anæmia rapidly decreases, especially under effective quinine treatment; the same is the case after severe infections when promptly and properly treated. In both, however, when improperly treated, a lasting form of anæmia may arise, which is characteristic of chronic malarial infection. In this condition the parasites are still in the circulatory system. This is important as leading to long-lasting residual infection and relapses.

Generally there is a *marked reduction in the total amount of hæmoglobin*, especially in sub-tertian infection. This reduction is not, however, of prognostic importance, as in some serious pernicious cases it may be only slight, and in some mild cases of benign tertian it may be considerable. Usually, as the case recovers, the deficiency of hæmoglobin is made up, but in cases of chronic malaria and malarial cachexia it may continue for months or years.

We have already referred to a form of perniciousness occasionally met with, due to the intense severity of the anæmia in malaria (p. 193). Rarely we find another change in severe cases of malarial infection—a condition simulating pernicious anæmia with poikilocytosis, and all the characteristic histological changes of the blood of that disease. These cases are always difficult to cure; many of them prove fatal, often from some intervening complication.

The leucocytes.—These are changed as regards total number in the surface blood, and in the relative proportions of the different varieties. A few hours from the beginning of a paroxysm there is a marked leucopenia, the number being from 3,000 to 5,000 per cubic mm. of blood, instead of 8,000 or 9,000, and the ratio of white to red cells changes in the apyretic interval from the normal to about 1 to 500, or even 1 to 900. But sometimes in the course of the attacks there may be an actual increase in the total number of white cells, *e.g.* a true leucocytosis may occur in the early stage of an acute attack, especially in malignant tertian malaria, and it may continue for a longer time in pernicious cases, while the temperature is rising. There may also be daily transient post-malarial leucocytosis in patients who have been treated by quinine.[1] As a rule, in the apyrexial period the polymorphonuclear cells fall from normal to 50 per cent., and the mononuclears (taking all forms collectively) rise from about 25 to about 45 per cent. of the number of leucocytes observed. The mononuclear percentage varies inversely with the temperature (D. THOMSON): when the temperature is rising the numbers of mononuclears

[1] S. P. JAMES's article, "Malaria Pathology," in BYAM and ARCHIBALD's *Practice of Medicine in the Tropics*, Vol. II, p. 1573.

the possible modifications in the pyrogenetic processes may be very complicated, and that some of them are ill understood.

The various stages of *the paroxysm* have been described (pp. 178–83). They form an extraordinary and abrupt aberration from the normal, and lately have been likened to the anaphylactic process. The symptoms accompanying the fever are said to be a consequence of an anaphylactic or *hæmoclastic* shock caused by the sudden entry into the plasma of freed parasites, which act as foreign colloidal substance. The usual signs of hæmoclasis are—a lowered arterial tension, leucopenia, alteration of the differential count, diminution *in the number of red cells, fall in the serum refractive index, and increased* coagulability of the blood. ABRAMI and SEVENET, quoted by S. P. JAMES,[1] "have ascertained that benign tertian paroxysms are preceded by a hæmoclastic crisis evidenced by these signs. They regard the chill, the vomiting, the backache, the headache and other symptoms of the cold stage of a malarial paroxysm as manifestations of this hæmoclastic shock."

Blood changes, anæmia.—The first effect of malarial infection is naturally most pronounced upon the blood, in which fluid the plasmodia live parasitically on the red cells, and in their metabolism manufacture toxins which considerably affect all the constituents of the blood. The pigment created leads to the condition of melanæmia, which has for the last seventy-five years been recognised as *one of the most characteristic pathological conditions in malarial infections.* The anæmia is frequently sufficient to manifest itself clinically. This is, to a large extent, the direct result of the destruction of red cells by the parasites; it is highly probable that some of the uninfected erythrocytes are likewise destroyed by the action of some form of hæmolysin, a soluble part of the toxins. The anæmia during the first attacks is marked, though rapidly remedied; during the following attacks it is not so conspicuous, but less speedily disappears. With the decrease in the number of erythrocytes there is often a *lowering of the colour index.*

As just stated, more red cells are destroyed than those invaded by parasites. If only infected cells were destroyed, they could readily be made up by the *latent physiological hæmogenic margin, but this is inadequate to meet the rapid* loss in malaria. Sometimes after a group of severe paroxysms, or after even one pernicious attack, there may be a loss of 1,000,000 red cells per cubic mm., and this may continue after each group of paroxysms until there are only 1,000,000 red cells per cubic mm. In the apyretic intervals red cells are rapidly restored.

In chronic malaria there is always a considerable decrease in the total number of white as well as of red cells.

It has recently been shown that there is a rise in the number of red cells to the extent of 10 to 30 per cent. after the inoculation of active malarial blood, followed by a fall.[2]

"Malarial oligocythæmia is accompanied by changes in the red cells themselves, *such as poikilocytosis, anisocytosis, and other signs of degeneration of* red cells."[3]

The largest destruction of red cells occurs during the early paroxysms. The destruction is greater in malignant tertian than in benign tertian and quartan malaria. After a certain degree of anæmia is arrived at, the destruction becomes gradually less. It is recorded that the number of red cells may be reduced to 2,000,000 per cubic mm. in four days; in one case after several attacks

[1] Article, "Malaria Pathology," in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics,* Vol. II, p. 1672.

[2] *British Medical Journal,* October 4, 1924, pp. 620, 621.

[3] MANSON'S *Tropical Diseases,* 8th Ed., p. 69.

degree of splenomegaly in children is not often met with in the young children in hyperendemic villages, and while the long stage of acute infestation lasts (pp. 42, 43).

Much destruction of red cells, both infected and non-infected, is said to occur in the spleen, and this is held by some to be partly responsible for the malarial anæmia. The large number of pigmented macrophage cells in the splenic sinuses is a striking feature of the pathology of sub-tertian malaria[1]; this is not a special macrophage distinct from other phagocytic cells.

Many infected red cells, and often non-infected cells also, are engulfed by phagocytic cells in the spleen. The spleen filters off many of the infected corpuscles; it gives rise to some of the macrophages and other phagocytic cells. From this it is easily understood why parasites and melanin are, as a rule, met with in large amounts in the spleen. Parasites may sometimes be found in the spleen when they have been absent from the peripheral blood.

In general, the longer the continuance of the paroxysms, the more frequent the repetitions of the fresh infections, and the more lasting the relapses, the greater are the hypertrophy and the induration of the spleen. With the earlier paroxysms the spleen is soft, retains its normal shape, has a sharp anterior margin, and on deep inspiration extends only slightly, if at all, below the left costal margin. Pressure from behind forwards on the left lower false ribs may render a slightly enlarged spleen palpable, especially in children. The increase in size of the spleen with each paroxysm, and its partial recession during the intervals, may often be distinctly recognised in hospital cases. In chronic infections the spleen may be enormously hypertrophied. But in very malarious places, within three months of birth a high proportion of infants may have big spleens, even when taking quinine for the malaria causing this condition.

Enlargement of the spleen of recent origin does not, as a rule, give rise to pain, though in many cases the organ is tender on palpation. Sometimes, however, pain is complained of, and may be of a sharp shooting character, similar to that of the first stage of acute pleurisy. This is probably due, in some cases, to perisplenitis, in others to stretching of the capsule, in others again to localised inflammation of the splenic parenchyma. The writer has seen many cases of this last-mentioned condition operated on and drained successfully. He recalls a case of splenic abscess in a boy of about ten years suffering also from cancrum oris of the left cheek, who died from the general effects of malarial cachexia and sepsis combined. As stated before, in chronic malaria there is increased susceptibility to secondary septic infections. The largest malarial spleens are naturally found in endemic malarious centres, where the inhabitants are constantly exposed to re-infections during the malaria season, and suffer from relapses during the non-malarious part of the year. Should these patients not succumb and eventually acquire a relative immunity, the spleen may once more disappear beneath the left costal arch, though it is more likely that some small degree of enlargement will be permanent.

Enlargement of the spleen indicates some degree of tolerance to the fever-producing toxin; in endemic malarial areas many persons free from fever have parasites in the blood. It seems to be one of the first efforts to bring about immunity. Sir MALCOLM WATSON[2] reminds us that SYDENHAM stated[3]: "It is worth noting that when thofe Autumnal Agues have a long time molested Children there is no hope of recovery till the Region of the Belly, efpecially about the Spleen, begins to be harden'd and to fwell; for the Ague goes

[1] MANSON, *Tropical Diseases*, 8th Ed., p. 58.
[2] *Prevention of Malaria in the Federated Malay States*, 2nd Ed.
[3] Dr. THOMAS SYDENHAM, *The Whole Works of*, 1735, chap. v. "Of the Agues, 1661–64."

increase. The largest number is found in the period between the paroxysms, when they may rise as high as 80 per cent. of the total leucocytes. The increase is mainly in the large mononuclears.

These percentages are not accepted by some malaria workers. All agree, however, that the true large mononuclears (histiocytes) are increased; the difficulty is to distinguish them from others like them.

Other cells.—Certain cells absent in normal blood may appear during the paroxysm, and these may be of diagnostic value. The chief are macrophages, 15 μ in diameter. They are oval or circular in shape, with hyaline protoplasm; they form a group of cells not always easy to diagnose from true large mononuclears. When oval the nucleus is eccentric and reniform; when circular, central and rounded. Endothelial cells, shed from the blood vessels (the so-called *reticulo-endothelial cells*), are large and irregular, with hyaline protoplasm and sometimes vacuolated. These cells may contain entire red cells, broken-up red cells, disintegrated parasites and melanin.

Phagocytosis.—The hæmozoin, breaking-up parasites and red cells are taken up by all varieties of leucocytes except the lymphocytes. Many red cells, both infected and non-infected, are removed from the circulation by phagocytic cells in the spleen.

Hæmozoin.—This, the only characteristic pigment of malaria, is first seen as small brown or black granules or rods in the parasites in red cells. When sporulation occurs the pigment is taken up by the leucocytes and other phagocytic cells, and is distributed in the tissues and organs of the body, but especially in the spleen, liver, brain and bone-marrow. For further remarks on hæmozoin see pp. 229, 230.

Post-malarial anæmia.—Cases occur in which, notwithstanding the abrogation of pyrexial attacks, the anæmia tends to increase. These may be seen in every endemic area. The condition is sometimes well marked in Europeans arriving at hill stations from the plains after suffering from severe malarial fever for some time. It has been called *post-malarial anæmia*, and is specially seen in Indian villages in the late autumn in ill-nourished people beyond middle life, and may be very marked in nursing mothers. The essential pathological nature of these cases has not been completely worked out. BIGNAMI [1] describes four different types of this anæmia.

Enlargement of the spleen.—This is an invariable accompaniment of the malarial paroxysm, though in the earlier paroxysms it may not be sufficient to be manifest by palpation. It is usually appreciable by physical examination whenever malarial paroxysms have continued for a week, especially in children. In chronic malaria and malarial cachexia the spleen may nearly fill the abdomen. In each paroxysm the spleen becomes hyperæmic, tender, enlarged, and sometimes painful. In every untreated case of malaria it may be felt on palpation a few days after paroxysms start, in children sometimes after the first paroxysm. This acute swelling is due partly to hypertrophy of the reticulo-endothelial cells (pulp cells—splenocytes) and to distension of the organ with blood, probably partly from reduced vaso-motor tone, which is so marked in the vessels of the chylopoietic viscera; later on, however, it is in part due to hyperplasia.

In chronic relapsing cases which have had little or no quinine treatment the spleen enlarges progressively, and may reach below the umbilicus to the left iliac crest. When proper quinine treatment is early adopted the enlargement is kept in check. In Indian villages, with severe endemicity, a high percentage of the children possess a much-enlarged spleen. Curiously, this

[1] NOTHNAGEL'S *Encyclopædia of Medicine*, Vol. XIX, MARCHIAFAVA and BIGNAMI, "Malaria," p. 1152.

lead to hypertrophic or atrophic cirrhosis with its clinical sequelæ. In these enlarged and congested malarial livers we get the condition of siderosis.

The chief structures affected are the capillaries, parenchymatous cells and connective tissue. The capillaries contain large numbers of macrophages, endothelial cells (hypertrophied and desquamating Kupffer cells of the "sinusoids" or liver capillaries) and much hæmozoin. The liver cells may be atrophied or even necrosed in patches, and frequently contain hæmosiderin. Fatty degeneration in central areas may also be met with. For further remarks on the morbid histology of the malarial liver see section on PATHOLOGICAL ANATOMY.

Nervous system.—The nervous system is involved more or less in every attack of malarial fever. In the premonitory symptoms of a paroxysm (p. 178) we may have depression and apprehension. In the hot stage some delirium is frequent. Headache, both frontal and occipital, is nearly always present. Backache and pains in the bones are sometimes severe. In very severe infections, especially malignant tertian, grave cerebral symptoms are sometimes present (p. 191), and in hyperendemic and epidemic outbursts of malaria we come across cases with aphasia, hemiplegia, paraplegia, convulsions, epileptiform attacks, hyperpyrexia, uncontrollable perspirations, etc. Temporary or enduring mental change may follow severe infestation; usually it takes the form of mental confusion, apathy, dullness and loss of memory; in others there is a state of restlessness, anxiety and tremors, with sleeplessness and hallucinations; very occasionally acute mania or melancholia may follow grave infections. The writer has treated cases of each of these three classes of mental change, and although the prognosis is good in some instances, especially among Europeans who have suffered for years with infections and re-infections, it is most gloomy as regards complete ultimate recovery, unless prolonged change to a non-malarial climate can be taken before the condition has gone too far. In the more chronic cases neuralgia or neuritis of particular nerves is sometimes met with; occasionally the hyperalgesic areas correspond to the distribution of nerves from some segment of the spinal cord, the area involved being specially sensitive to light pinpricks.

Implication of the vaso-motor mechanism is shown during the paroxysm by the clinical manifestations of the cold and hot stages. Several of the symptoms associated with involvement of the nervous system arise from the packing of parasites and hæmozoin in the cerebral capillaries; others are due to the local action of toxins which cause degenerative changes in nerve cells and tissue, degeneration of the endothelial lining of vessels giving rise to punctiform hæmorrhages into the surrounding brain substance. In fatal cases capillaries and arterioles are usually blocked with erythrocytes containing parasites mostly in the sporulating stage (pp. 234, 235, and Plate XIII, 181, and Plate XIV, A 2, 5), many pigmented macrophages, endothelial cells and leucocytes. The writer has likewise found free parasites outside the blood vessels in the absence of any form of hæmorrhage. The parasitised cells tend to adhere to the inner lining of the vessels, and in severe cases cause thrombosis. Small hæmorrhages round the vessels are met with, but the red cells in these are not infected. The ganglionic cells in a large percentage of cerebral cases show signs of degenerative change—abnormal shape, granulation of the protoplasm, loss of chromatin in the nucleus, and absence of Nissl's bodies. It is important to remember, however, that cases with grave cerebral malaria occur in which there are few or no microscopical or macroscopical changes in the tissues of the brain. In the Punjab and United Provinces malaria epidemic of 1908 there were hundreds of these cerebral cases among our British and Indian soldiers, many with convulsions, that recovered under energetic intravenous quinine treatment; had they died, and had no post-

gradually off as this symptom comes on; nor perhaps can you any other way prognofticate the going off of the Difeafe in a fhort time, than by obferving this Symptom and the fwelling of the Legs, which are fometimes feen in grown people."

The enlargement of the spleen in chronic malarial infection may be so great as to give rise to considerable tension of the capsule; in this condition rupture of the spleen is liable to follow slight injuries or falls. Following such rupture there is extensive hæmorrhagic extravasation into the abdominal cavity and usually rapid death. Death may not, however, be immediate. The writer has recorded two cases where the victims of traumatic rupture of malarial spleen walked home and died after their accident.[1] In recent years cases of rupture of the spleen have been recorded as occurring in acute malaria, deliberately induced for the cure of general paralysis, and in these cases it seems possible definitely to exclude traumatism.

A rough classification of enlargements of the spleen adopted by the writer falls into six groups: (*a*) not palpable; (*b*) palpable one finger's breath below the left costal arch; (*c*) palpable two or three fingers' breadth below the left costal arch; (*d*) a hand's breadth (four inches) below the left costal arch; (*e*) still larger, reaching to the umbilicus; (*f*) to the crest of the left ilium or nearly filling the abdomen.

For microscopic appearances of spleen smears and sections see p. 232.

Digestive system.—Disturbance of the digestive system is constant in malarial attacks. At the beginning of the paroxysm the mouth is dry, the tongue more or less coated, and the appetite in all but slight cases decreased, or even lost. Nausea is often present, and sometimes there is troublesome vomiting, which is simple or bilious. Constipation is usual, and this with sluggish liver frequently leads the patient to believe he is suffering from a bilious attack or a "touch of liver." Diarrhœa is sometimes present, and may be extremely severe (pp. 189, 192). Occasionally, severe and intense pain in the upper region of the abdomen and symptoms of collapse are associated with acute malarial pancreatitis (p. 192). Decreased gastric secretion is considered to be a cause of the digestive troubles, and one of the causes of the diarrhœa when it is present. The persistent vomiting "may be in consequence of the cerebral anæmia which follows the rush of blood to the abdominal organs; or it may be a manifestation of an anaphylactic process" (S. P. James). When the intestines are specially attacked the capillaries of the mucosa and villi are blocked with infected red cells containing masses of pigment. In microscopic sections of the villi the writer has found large numbers of infected red cells—schizonts nearing maturity, others about to sporulate—outside the capillary walls and free. Hæmorrhages into the tissues of the mucosa and villi are common in these intestinal cases. There may also be extensive accumulations of infected red cells in the capillaries of the pancreas with small or large hæmorrhages and deposits of hæmozoin in the pancreatic tissue (p. 192, also Plate XIII, 132).

Enlargement of the liver.—In acute malaria of all types the liver is slightly enlarged and congested during the paroxysms, and it may be tender and associated with slight jaundice. It is a constant accompaniment in the variety of malignant tertian called *bilious remittent fever* (p. 189). In the intervals between the attacks the enlargement subsides. After a series of attacks the congestion may become chronic, if not permanent. In these latter cases, on post-mortem the capsule is tense, the cut surface congested and reddish brown in colour or verging on black. If this chronic malarial hepatitis is long continued there is thickening of the intralobular connective tissue, which may

[1] Hehir and Gribble's *Medical Jurisprudence for India*, 5th Ed., p. 183 *et seq.*

normal and the urine high-coloured from urobilin and urobilinogen. An evanescent albuminuria is often present towards the end of the hot stage, and in many severe malignant cases a trace of hæmoglobin, epithelial and granular casts are found. Nephritis is an uncommon complication, but it sometimes occurs, and may even be of the acute hæmorrhagic type with hæmaturia and a large quantity of albumin and epithelial casts in the urine. Occasionally red cells crowd the renal capillaries and there are pigmentation, hæmorrhages, and swelling and degeneration of the epithelium of the convoluted tubules (see also p. 233).

Muscular system.—In ordinary cases of malaria there is for some time little loss of weight or strength. Indeed, it is remarkable that we see so little real emaciation even in cases of *chronic malaria in endemic areas. The people* are not physically strong nor intellectually bright, but they are not emaciated like those suffering from kala-azar (p. 204). But those experiencing the epidemic form of the disease suffer greatly from muscular atony and general weakness, and lose flesh rapidly, and they take a long time to recuperate.

Suprarenal glands.—Malarial involvement of the adrenals is every now and then met with as a form of perniciousness in malignant tertian infection. It is almost pathognomonic clinically—great muscular prostration, very low blood pressure without any organic implication of the heart, pain in the back, severe headache, vomiting, diarrhœa, coma and death (see p. 233).

C.—CHEMICAL PATHOLOGY OF MALARIA

(*a*) **Malarial toxins.**—It is assumed by most authorities as highly probable that the parasites of malaria manufacture a toxin or toxins which are responsible for the paroxysms of fever. This was originally suggested by GOLGI. Up to date no toxin has been isolated. We assume that such poisons are elaborated as the only explanation of the extraordinarily complex clinical phenomena associated with a malarial paroxysm. The whole paroxysm indicates a sudden poisoning of the system followed by the elimination of some poison, while the rigor suggests that the entire system has been subjected to a shock. Many malariologists, indeed, consider the paroxysm to be a toxic anaphylactic shock. The cycle of the paroxysm, in its typical form, is embraced in the rigor, accompanied and followed by pyrexia, in turn succeeded by profuse sweating, with more or less sudden disappearance of all the pyrexial phenomena.

If in a case, say, of quartan infection we give a full dose of quinine two hours before the paroxysm begins, that paroxysm occurs, but the next paroxysm is often cut short, or may not occur at all. We assume that the young parasites are killed off by the quinine, which acts as a plasmodicide. For a long time we also assumed that there is a toxic poison formed by the parasite which is *pyrogenetic*. The existence of such a body has been proved. We shall see that there is also a *hæmolytic toxin*. There are, therefore, almost certainly two toxins—one pyrogenetic, the other destructive to the red cells. There is probably also an *endotheliolysin*. It is not improbable that other toxins will be discovered, especially one or more *capable of acting on the vaso-motor* system and interfering with thermolysis.

Pyrogenetic toxin of malaria.—The occurrence of toxins in malaria was for a long time inferred as part of the intimate pathology of malarial infection. Notwithstanding the importance of the subject, the actual experimental work in connexion with malarial toxins has been comparatively meagre.

mortems been held, they would have been called "cerebral malaria." The writer performed several post-mortems on European seamen admitted into the Presidency General Hospital, Alipore, Calcutta, with cerebral symptoms from malignant tertian malaria, in which no histological or gross lesions were found in the brain.

Circulatory system.—Except in the most serious cases cardiac involvement is seldom obvious, but in many of the graver infestations weakness and dilatation with palpitation and precordial pain are met with. Murmurs are common. In the class known as *cardiac perniciousness* (p. 191) the cardiac muscle fibres may be found to contain free parasites outside the blood vessels; fatty degenerative changes may also be met with (p. 231). In the more persistent cases with relapses tachycardia may continue for a long time.

The blood vessels are affected in all malarial attacks, directly by the action of the toxins of parasites and the parasites themselves, and indirectly through the vaso-motor nerves. It is not surprising, therefore, that hæmorrhages are common in the more serious infestations—from the bowels, kidneys, into the cortex of the brain, and pancreas. Some loss of vascular tone is present in all attacks. Even in the hot stage the minimum blood pressure is decidedly below normal. The fall in blood pressure is greatest soon after the paroxysm begins, but continues in the apyrexial intervals between relapses, sometimes for long periods. The average pressure may then not be more than 80 or 90 mm. This fall of pressure is probably not due to damage to the heart muscle or cardiac debility (S. P. JAMES). But there are cases in which diffuse fatty degeneration of the heart takes place (p. 231). The clinical symptoms of these cases are those met in acute cardiac failure. The fall in blood pressure is said by some to be due to the action of parasites on the vaso-motor nerves, by others it is considered to be part of an anaphylactic process, by others again it is thought to be due to lesion of the suprarenal glands.

Skin.—The goose-skin which occurs in the cold stage of a paroxysm may be caused by some malarial toxin acting on unstriped muscle affecting the erectores pilorum innervated by the sympathetic.

When there have been many attacks the skin in Europeans becomes sallow, with patches of pigmentation; in Indians the pallor of the mucous membranes is conspicuous, with black or dark brown patches; the normal colour of the skin is darker, and pigmented patches are very obvious. Labial herpes is very common, usually following the first or second paroxysm. In chronic cases, especially if there is much anæmia, œdema of the ankles and feet occurs; in the cold weather these cases suffer from cold feet, and in winter in the higher hills the writer has met some cases of gangrene of the toes and one case simulating Raynaud's disease in a Gurkha soldier; these persons were in an exceedingly bad state of health and heavily impregnated with malaria acquired in their homes at the foot-hills in Nepal while on leave.

Respiratory system.—In the milder forms of malaria it is rare for any lung symptoms to appear. In severe cases there may be dyspnœa and slight bronchitis. In serious infestations, especially those occurring in relapses, true croupous pneumonia may occur (see p. 238).

Urinary system.—A certain amount of polyuria always precedes the hot stage, and may continue throughout the whole paroxysm. It arises, partly at least, from the vaso-motor contraction of the cutaneous blood vessels during the cold stage, with hyperæmia of the kidneys and rise of blood pressure in them. The urine at first is pale, but later is high-coloured and contains more urates and phosphates than normal. In severe attacks the urea is much above

within the red cells this pyrogenous material does not affect the temperature. It is only when it is set free after sporulation and reaches the special nerve centres connected with heat regulation that this influence is exerted. The toxins of malarial infection appear to have a special affinity for the nervous system, and this explains many of the clinical phenomena of malarial fevers and their sequelæ. Indeed, the entire paroxysm of malaria is in all probability due to the effect of a poison on the nervous system. The paroxysm is the clinical manifestation of the reaction of the nervous system to the malarial toxin circulating in the blood—a regular intoxication. Many of the nervous symptoms seen in malarial fevers show us that all parts of that system share the effects of this intoxication, which is first manifest in its action on the vaso-motor centres. In the cerebrum we have every degree of effect from slight stupor to coma, from minor depression to active delirium; headache more or less is associated with every paroxysm; neuralgia often occurs, especially in the second and third divisions of the fifth cranial nerve.

Hæmolytic toxin of malaria.—Hæmolysis in malaria was referred to on p. 219 under *malarial anæmia.* CASAGRANDI and DE BLASI have described what they consider to be a hæmolytic toxin. They state that a hæmolysin is set free on sporulation, damages the erythrocytes and gives rise to the formation of hæmosiderin. This is deposited in the parenchyma cells of organs, *e.g.* the liver, and may perhaps damage them. The hæmolysin is said to cause a solution of the hæmoglobin in the serum. That some kind of hæmolytic action occurs *in vitro* is observed in fresh specimens of malarial blood that have been carefully ringed with vaseline. We notice under the microscope that the serum acquires a darker yellow colour the longer the fresh blood is kept under observation, and the red cells become more and more embedded in the plasma. CASAGRANDI considers that his experiments on Halteridium seem to indicate that an analogous material checks the multiplication of that parasite in birds.

DE BLASI believes that in human malaria an anti-hæmolysin is generated in the body, and that it is possible that this body has the power of checking to some extent the multiplication of the parasites.

The parasites seem, then, to have some kind of hæmolytic action, so destroying red cells and throwing additional labour on the overworked liver. The result is excessive bile production, with bile in the urine and, it may be, diarrhœa. If the detritus of the red cell destruction is beyond the capacity of the liver to deal with, some of it may pass through that organ and give rise to hæmoglobinuria. An antitoxin, it is stated by some authorities, is quickly formed to neutralise this hæmolytic action, and may quickly lead to cure of the disease.

The question of a hæmolytic action, however, is not so simple as the foregoing statements seem to indicate; it is highly complex and still *sub judice*; the best authorities on malaria and blackwater fever even deny the presence of a hæmolysin in malarial blood. It is fairly easy to extract from *normal* red cells hæmolytic bodies (lipoids) which act *in vitro*, and in fact, by washing red cells in phosphate these bodies can be removed, so that the cells are rendered more resistant (BRINKMAN and others). The extraction of a hæmolytic body is no proof of a malarial hæmolysin. Again, a hæmolysin must be distinguished from a hæmolytic body: a hæmolysin requires a complement for its action. S. R. CHRISTOPHERS states: "Many observers have tried to demonstrate the presence of hæmolysins in malaria or in blackwater fever, but so far without real success . . . they are mainly demonstrations of different effects resulting from normal isolytic properties of human blood . . . with which the observers were insufficiently or not at all acquainted."

The experiments of MANNABERG,[1] CELLI,[2] MONTESANO and GUALDI were negative.

Some very suggestive experiments regarding the existence of a malarial toxin were carried out by ROSENAU, PARKER, FRANCIS and BEYER.[3] These experiments show that there is in malarial blood during the first and second stages of the paroxysm, that is, before the temperature begins to fall, a toxin which is manufactured by malaria parasites, and that this toxin is responsible for all the phenomena of a malarial paroxysm. These workers injected into the veins of healthy people blood taken from cases of malarial fever at different stages of the malarial paroxysm, the blood being defibrinated and in some instances filtered through a Berkefeld or a Pasteur-Chamberland filter, in others unfiltered.

These experiments, conducted with scientific care and precision, point to the existence in the blood of a pyrogenetic toxin during the early stage of a malarial paroxysm, and the inference is strong that this toxin is liberated from the red blood cells at the time the spores are set free. It is also highly probable that the toxin is soluble in the plasma of the blood, and continues in solution in the serum after this has been separated from the fibrin and blood corpuscles. It would seem that the malarial toxin, after disturbing the thermotaxic mechanism by increasing thermogenesis and lessening thermolysis, is either eliminated, or its effects neutralised, by an antitoxin generated in the blood. At the initial stage of each malarial paroxysm a fresh quantity of toxin is liberated into the plasma and the whole of the phenomena of a paroxysm commenced. It is almost certain also that the malarial toxin is responsible for at least part of the degenerative changes met with in the parenchymatous cells of the spleen, liver, kidneys and brain in cases of lasting malarial infection.

So far as can be ascertained the highly interesting experiments referred to above have not been repeated, and call for confirmation. There are unrivalled facilities for conducting such experiments in India, and the writer takes this opportunity of suggesting that the work of ROSENAU, PARKER, FRANCIS and BEYER be repeated in the Calcutta School of Tropical Medicine. With the aid of an expert biochemist in such an inquiry, it is highly probable that the actual toxin or toxins of malarial blood would be isolated. Simultaneously the nature of the antitoxin (if one is manufactured) of malarial blood could be inquired into, and FORD's work[4] re-investigated.

It is now well known, because proved by several observers independently, especially by C. W. DANIELS, that blood serum taken just before the rigor stage of a paroxysm and passed through a Berkefeld filter, will, when injected into a healthy man, cause a febrile paroxysm resembling malaria. There are weak points in these groups of experiments. It is now known that a solution of hæmoglobin very carefully freed from stromata will produce slight febrile disturbance—some shivering and malaise—in man. Artificial preparations of hæmatin will, in rabbits, produce a condition simulating the rigors of a malarial paroxysm.

The pyrexial phenomena of malarial paroxysms have been satisfactorily explained, but not with the same degree of precision as the anæmia and melanæmia. The parasite in its growth in red cells produces a pyrogenetic material which is set free when the red cells burst during sporulation, and is capable of disturbing the thermotaxic mechanism, probably mainly by increasing thermogenesis, and to a less extent by lessening thermolysis. While

[1] *Experimental Studies in Yellow Fever and Malaria*, p. 92.
[2] *Malaria*, p. 231.
[3] *Experimental Studies in Yellow Fever and Malaria* (1910), Yellow Fever Institute Report.
[4] *Medical Record*, Vol. LXVI, p. 1001.

to distinct coloration which varies from reddish brown to black, in accordance with the quantity present.

When from any cause death occurs some time after cessation of paroxysms, melanin has a more restricted distribution. It is absent from the red and white cells and from endothelium, but is found in the parenchyma of the spleen and connective tissue cells of the liver. It is now in larger masses, though these may be seen to consist of separate granules. Still later it is found as blocks, and the cells containing it do not take basic stains, being seen only in outline round the mass of melanin. Still more remotely, say a few years after, if found it will be seen embedded in the trabeculæ, and the cell structure has disappeared; the spleen is then the only organ that contains melanin.

"Pigment is most abundant in the splenic vein. In other vessels it is found to be included in ordinary leucocytes, in the splenic vein it is included in large white cells, probably identical with splenic pulp cells. The explanation is that the spleen is not only the physiological destination of the hæmozoin-laden leucocytes, but is a favourite nursery of the parasite."[1]

Eventually hæmozoin disappears from the body, being partially digested by phagocytes and tissue cells, and partially removed by the lymph, but much more work will have to be done before we can tell the whole story of how it finally vanishes. The process of its disintegration, if continued, irritates the tissues.

The reason why some varieties of parasites are found uniformly distributed and others not, and why red cells containing pigmented parasites tend to accumulate in the capillaries of internal organs as described, has not been definitely ascertained. It is discussed (*passim*) in this volume.

It will thus be seen that the pigment of malaria affects practically all the cells of the body. There is in addition a process of *necrobiosis* affecting the parenchyma of internal organs. This necrosis is mainly caused by stasis in the capillaries, to a less extent probably by the action of toxins. The necrotic particles are finally removed in the same way as in other diseased conditions.

Melanin is insoluble in alcohol, ether, acids or water; it is readily dissolved by alkalis and is specially soluble in ammonium sulphide. In solution in alkalis it has a greenish tinge, but has no distinctive bands when examined spectroscopically. It is rich in iron, which is in firm organic combination, and does not give the Prussian blue reaction, but, when treated with "unmasking" reagents, *e.g.* ammonium sulphide, does so. Formalin acting on hæmoglobin gives rise to a black deposit that may be mistaken for hæmozoin; it should not, therefore, be used as a preserving or fixing fluid for malarial tissues or organs.

(ii) **Hæmosiderin.**—Besides hæmozoin manufactured by the parasites in the blood, there is another form of pigment in malaria which is yellow or ochre-coloured, called *hæmosiderin*. It gives the Prussian blue reaction. The term hæmosiderin probably covers a variety of allied pigments—hæmosiderins, hæmosideroids—having different colours and reactions. It is found as yellow granules in the spleen, liver, bone-marrow, kidneys, pia mater, pancreas and thyroid gland. Rarely it is found in the circulating leucocytes and vascular endothelium. This pigment is derived from the hæmoglobin of red blood cells that has not been entirely absorbed by the parasites. More of it is naturally formed from the red cells infected by malignant tertian parasites, which only partly fill the red cells even when sporulating, and in segmentation a large part of the hæmoglobin of each infected erythrocyte is discharged into the plasma. It has also been noted that in all probability a large number of uninfected

[1] MANSON, *Tropical Diseases*, 8th Ed., p. 60.

Endotheliolytic toxin.—Another toxin stated to be manufactured by malaria parasites is *endotheliolysin*. This is said to injure the endothelial lining of capillary blood vessels, the slow flow of blood through them permitting this action, and through the change in the endothelium the infected red cells are caught up in the capillaries. The toxins of quartan parasites do not appear to damage the endothelium in this way, hence they pass through all parts of the circulatory system freely.

The degenerative changes in the cells of nerve centres and the necrotic condition of renal epithelial cells, apart from the effects of stasis, lend support to the existence of malarial toxins. The toxins are being constantly excreted during malarial infection in large or small quantities. The parasites certainly do decrease spontaneously, and this is probably due to some plasmodicidal agent created in the blood which acts deleteriously and specifically on the young parasites outside and inside the red cells, possibly in the same way that quinine does. It is considered by some authorities that the parasites attempt to neutralise the assumed plasmodicidal action of the serum; the evidence brought forward to uphold this view is in no way convincing. (See pp. 44, 45, 214 and 215.)

(*b*) **Pigments found in the body in malaria.**—We may now consider certain pigments that are formed in the body in malaria—melanin, hæmosiderin, hæmofuscin, etc. Melanin alone is exclusively malarial in origin.

(i) **Melanin, hæmozoin, or malarial pigment.**—Hæmozoin is the residue from the digestion of the hæmoglobin of erythrocytes by the plasmodia of malaria. *It is the only pigment that is characteristic of malaria*; it is the special product of parasitic metabolism. In acute malaria melanin is found in parasites, in leucocytes, in the parenchyma of the spleen in certain connective tissue cells of the liver,[1] and sometimes in the nuclei of the endothelium of the capillaries of the brain, liver, suprarenal glands, etc. It is met with at any time during a malarial infection, so long as parasites continue to develop in the blood. The best time to search for it in the blood is during or shortly after the paroxysm. It may also be found after paroxysms have ceased, so long as gametocytes are in the circulation. Provided there are no gametocytes in the circulation, no melanin is to be found in the blood beyond forty-eight hours after the last paroxysm. This is of prognostic importance as indicating, anyhow for the time being, a cessation of the effects of the infection.

The hæmozoin, after it has been set free from the disintegrated parasites and fragmented red cells, is contained mainly in the large mononuclear cells (macrophages) and the endothelium of the capillaries, and also in the polymorphonuclear cells.[2] It appears in the form of brown or brownish black pigment, in granules, grains, clumps or irregular blocks. This pigment is the most characteristic product of malarial infection, and is merely that formed within the parasites.

The hæmozoin set free by sporulation plays an important part in malarial fevers. The granules and blocks, after rapidly being taken up by the phagocytic cells—wandering and fixed leucocytes and vascular endothelium—are transferred to the connective tissues of the liver, spleen and other internal organs.

In acute malaria melanin will be found in any organ, mainly in those in which sporulation chiefly takes place—spleen, liver, bone-marrow—giving rise

[1] Certain connective tissue fibres of the liver—the reticular tissue—are different from ordinary connective tissue fibres in staining reactions and yield no gelatine on boiling; these are the reticulum fibres with which Kupffer's cells are associated.

[2] Pigmented leucocytes may be abundant in the first drop of blood *from the ear*, scanty or absent in the following drops.

D.—PATHOLOGICAL ANATOMY OF MALARIA

Morbid anatomy of enlarged spleen in malaria.—The spleen is always enlarged, but to a varying degree; it may be just palpable or almost fill the abdomen. In acute malaria its consistency is lessened, the parenchyma being sometimes very soft. Usually, however, the enlarged spleen is firm, often very dark, even black if the post-mortem is made soon after death. It is not diffluent, as is usually stated. During the writer's ten years as pathologist to the Afsul Gunj Hospital, Hyderabad (Deccan), in several hundred post-mortem examinations of malarial spleens he did not meet with one that was diffluent, except as the result of putrefactive changes; such putrefaction sets in very early, especially in the hot weather. In chronic malaria we get the hard ague cake.

The colour differs. The surface is dark; the substance varies from dark brown or chocolate to a slaty or black colour, this hue being usually diffuse. The section is of a dark greyish brown, and the non-pigmented Malpighian bodies stand out clearly. The capsule in acute cases is thin, stretched and easily torn; in chronic cases it may be thick and firm, and adherent in patches to apposed parts. The splenic septa and reticulum are thickened. (See Appendix VI—8, 9.)

Spleens much hypertrophied from malaria are very liable to rupture from blows or falls on the abdomen. The writer has carried out many post-mortem examinations on cases of traumatic rupture of the malarial spleen, and has recorded elsewhere the details of six of them, all in Indians.[1] As already noted, spontaneous rupture of the spleen in acute malaria can, as the result of deliberate infection of general paralytics, no longer be questioned.

Microscopic appearances of spleen smears and sections.—The chief microscopic appearances in smears or sections of a malarial spleen are: (*a*) red blood corpuscles containing parasites in various stages of development; (*b*) a large number of phagocytic cells, including giant macrophages and endothelial cells; (*c*) an abundance of true malarial pigment occurring as granules, rods, blocks or masses in phagocytic cells, and also free in the various sinuses; (*d*) golden yellow pigment (hæmosiderin) derived from destroyed red corpuscles; (*e*) evidence of phagocytosis of red blood corpuscles; (*f*) thrombosis of capillaries; (*g*) local necrosis of the spleen pulp, including the Malpighian bodies; (*h*) congestion and distension of the splenic sinuses with blood (S. P. JAMES)[2] (see Plate XIII, 130, and Plate XIV, A, 4). No one can recognise half the bodies seen in spleen smears.

Morbid anatomy of enlarged liver in malaria.—The liver is usually enlarged, softened, congested and pigmented. The pathological appearances are due to pigmentation and congestion. Its colour on the surface varies from a steel-blue or olive-grey to chocolate, or even deep brownish black. The capillaries of the portal and hepatic veins, and the branches of the hepatic artery, are seen microscopically to be packed with parasites. The branches of the portal vein contain splenic macrophages, which may be sufficient in numbers to block the capillaries—macrophages are not seen in the branches of the hepatic veins. The hepatic cells are enlarged, frequently contain hæmosiderin, rarely melanin, sometimes the remains of red cells (BIGNAMI).[3] The endothelial cells of the capillaries are often swollen; this swelling may even include the vessels, and these cells are often packed with melanin, as may also be the swollen Kupffer's cells, which are charged with black pigment. The pigment is chiefly in the periphery of the lobules, and in blocks in the perivascular connective

[1] HEHIR and GRIBBLE, *Outlines of Medical Jurisprudence for India*, 5th Ed., pp 197 *et seq.*
[2] BYAM and ARCHIBALD's *Practice of Medicine in the Tropics*, Vol. II, p. 1576.
[3] MARCHIAFAVA and BIGNAMI, *Malaria* in *Twentieth-Century Practice of Medicine*, Vol. XIX.

red cells are destroyed (necrosed and broken up) by the action of a malarial hæmolytic toxin. The actual method of formation of hæmosiderin from hæmoglobin is not as yet definitely known. "Whether the fragments of the red cells are taken up as such by the parenchymatous cells and transformed into this ochre-coloured pigment, or whether the hæmoglobin of these fragments infiltrates the cells in a dissolved condition and is there precipitated in this form, is a question which in our opinion may be answered by the assertion that both probably occur. The further fate of this pigment is only partly known." [1]

It is considered that the liver cells metabolise part of this pigment into bile, which would explain the large discharge of bile, by vomiting and in the fæces, met with during malarial paroxysms.

Hæmosiderin, then, is not peculiar to malaria; it may occur wherever there has been marked blood destruction—in hæmoglobinuria, pernicious anæmia, poisoning by such agents as chlorate of potassium and pyrogallic acid. The subject of hæmosiderin is a much more complex one than textbooks indicate.

We have seen that the main effects of malaria—pyrexia, anæmia and melanæmia—can now be partly explained.

Polycholia.—The liver can deal with a certain amount of free hæmoglobin in the blood by increased secretion of bile. If the bile formed is excessive we get bilious symptoms—vomiting of bile and bilious diarrhœa, which are common in malaria, especially in bilious remittent fever.

(iii) **Hæmofuscin** is another pigmentary deposit of a dirty colour frequently found in internal organs in malaria; it is, however, also met with in the anæmia of ankylostomiasis, pernicious anæmia, and other conditions in which blood destruction occurs, *e.g.* kala-azar, blackwater fever and trypanosomiasis. It is insoluble in alkalis and acids, but slightly soluble in alcohol; it does not usually give the reactions of inorganic iron. It is found in the parenchyma cells of the liver, the secreting cells of the kidneys, and in the spleen. It is seen in sections in the cells of these organs without staining, but with carmine stain both it and melanin (if present) are displayed against the red background.[2] Like the other pigments, hæmofuscin is still under inquiry.

(iv) **Urobilin in malarial attacks.**—There is increased excretion of urobilin in the urine and stools, and its quantity bears a direct relation to the severity of the attack in recent infections, and as a rule gradually diminishes. Urobilin is, of course, a normal urinary pigment, but is increased in malaria. The duration of the increase and its amount vary in different cases. It may be found in convalescence when attacks have ceased. More is present in the stools than in the urine, and it lasts longer in them. But urobilin may occur in healthy persons, hence in the absence of anæmia and hypertrophy of the spleen it is no proof of latent malaria. Its amount and nature are the same in all types of malarial fever. Quinine treatment does not affect it. It persists after the parasites have been driven out of the peripheral circulation. It is in largest amount during the decline of the fever, and in the intervals. There is little correspondence between the urobilin excreted in the urine and stools and the hæmoglobin loss.

(v) **Urobilinogen.**—This substance is found in the urine in practically all cases of malaria.

[1] MARCHIAFAVA and BIGNAMI, *Malaria* in *Twentieth-Century Practice of Medicine*, Vol. XIX.

[2] DANIELS and NEWHAM'S *Lab. Studies in Trop. Med.*, 5th Ed., p. 190.

writer demonstrated that in a fair percentage of cases of malarial fever of all types the urine contains hæmoglobin during the paroxysm. In heavy infections there is an excess of bile pigments.

Heart in malaria.—In malaria cases DUDGEON and CLARKE have found diffuse fatty degeneration of the heart in all respects like that seen in death due to diphtheritic toxæmia. Of 45 fatal malaria cases in which the myocardium was examined, slight fatty degeneration was found in 15, moderate in 3, and diffuse in 5. In 7 of these cases the cardiac capillaries were loaded with parasites, and thrombosis of the vessels was noticed in 2 cases. These cases of diffuse fatty degeneration are clinically associated with symptoms of acute heart failure. The writer has recently seen a series of microscopic sections displaying small hæmorrhages around the thrombosed capillaries of the myocardium, and capillaries engorged with infected red cells, as well as sections of a malarial heart, showing parasites free in the striated muscle. He is strongly inclined to believe that all this involvement of the heart is a more serious factor in severe malarial infections than is generally recognised and may explain the sudden deaths sometimes met with in malignant tertian fever.

The series of sections mentioned came from a fatal malarial cardiac case with collapse during life, but without cerebral symptoms. In it "malarial parasites were found in the undifferentiated protoplasm round the nuclei of the cardiac muscle fibre, a fact which is believed to be of importance as indicating that this is a place where the parasites may be stored in quiescent periods between attacks."[1]

Blood vessels in malaria.—These are implicated through the effects of the toxins on the vaso-motor nerves, and also by the parasites in the lining walls of the vessels. We have seen that necrosis of vascular endothelial cells may lead to hæmorrhage; hæmorrhage may occur in the brain, spleen, nose, mouth, and even into the eyeball. Blocking of capillaries gives rise to blood stasis, more or less complete.

Nervous system in malaria.—Occlusion of the circulation in a large number of capillaries of the central nervous system in many cases of severe malarial fever explains most of the functional disturbance met with. The effects of capillary hæmorrhages resulting from blocking are inseparable from those of the blocking itself.

Brain and spinal cord in malaria.—The meninges may be thickened and œdematous and show punctiform hæmorrhages. Vessels of the pia mater and brain cortex are full. The surface of the brain may appear normal, but it is usually melanotic or lead-coloured from accumulation of pigmented parasites in red cells. The dark discoloration is nearly always visible to the naked eye. The grey and white matter of the cord is affected in the same way. There may be slight œdema with pigmentation and petechiæ, or pigment without patches in the substance of the brain (Plate XIII, 131).

Microscopically the *pigment*, usually uniformly distributed in the brain, may be scattered. When uniformly distributed the position of the pigment maps out the capillary blood vessels, being contained in red cells within the capillaries. Sections seem to show that the infected red cells are glued to the endothelial walls, and the healthy ones in the middle. Pigment is, however, also contained in the large mononuclears and in the endothelial cells; the swollen state of the latter cells helps to occlude the vessels and disturb the

[1] J. F. GASKELL and W. L. MILLAR, "Studies on Malignant Malaria," *Quarterly Jl. Med.*, 1920, p. 381.

tissue. The liver cells contain hæmosiderin, but no hæmozoin. Occasionally microscopic necrotic patches are seen, due to thrombosis. "Collections of small cells are not infrequently found in the tissue around the portal vessels, and this may be the earlier stage of a succeeding cirrhosis."[1] There is often some hyperæmia, to which, with the infiltration with pigment, the enlargement is due. The liver cells may be atrophied and contain hæmofuscin, while the melanin is contained in the interstitial cells. Great degeneration of the liver cells may occur in serious paroxysms of sub-tertian fever.

Bone-marrow in malaria.—The marrow of the spongy bones, such as the bodies of the vertebra, sternum and ribs, is congested, soft, almost diffluent, of a brownish red colour, due to extensive development of normoblastic tissue; gametes, macrophages and large mononuclear leucocytes are numerous, often partially degenerated. Parasites and melanin are free. Pigment disappears rapidly from bone-marrow. This is one of the areas in which crescents develop, especially in the ribs. "The rib-marrow especially seems to be the site of election for the development of the gametes of *P. falciparum*. Gamete forms in all stages of growth are frequently localised here, even when found scarcely or not at all in other places."[2] Hæmozoin is found in the blood vessels, as also in the parenchyma outside and away from them.

Lungs in malaria.—Large pigmented mononuclears in the capillaries, but especially in the veins; in the lungs phagocytosis is proceeding actively. There is in many cases a terminal infection with *Diplococcus pneumoniæ* (p. 225). Double hypostatic congestion may occur towards the end of fatal cases. The writer has often found free malignant tertian schizonts in various stages of development in the alveoli in broncho-pneumonic cases, and in the sero-sanguineous fluid in hypostatic cases. The effects of malaria on the lungs, and what goes on in them, call for much further careful observation.

Intestine in malaria.—When the intestine has been specially invaded the capillaries of the mucosa, including the villi, will be found packed with red cells containing parasites in all stages of development, together with phagocytes and leucocytes charged with blocks or masses of melanin (Plate XIII, 132). We may get hæmorrhages from the intestines, and at times hæmorrhages into the mucosa and villi, and patches of superficial necrosis of the epithelial surface. In pernicious cases of intestinal malaria free schizonts may be found outside the capillaries of the villi of the small intestines.

Suprarenal capsules in malaria.—In sub-tertian malaria these glands are nearly always implicated, especially in reduction of the lipoids of the cortex. This involvement may explain the great muscular weakness and low blood pressure met with in some cases of malignant tertian fever.

Kidneys in malaria.—Nephritis may occur occasionally as a complication, and in association with it there may be hæmaturia and epithelial casts in the urine. Changes may occur in the epithelium of the tubules independently of the presence of parasites. Usually the kidneys show no change; rarely we may find the renal capillaries packed with infected red cells in association with congestion, pigmentation and punctiform hæmorrhages, and swelling and degeneration of the epithelium of the convoluted tubules. The urine should be examined in all cases of malaria. In the more acute paroxysms of malignant tertian infection the urine may contain granular and epithelial casts. Slight hæmoglobinuria is not uncommon. About thirty-two years ago the

[1] MANNABERG, *Malarial Parasites*, p. 350.
[2] W. M. JAMES, *International Conference on Health Problems in Tropical America*, 1924, p. 69.

Serous membranes in malaria.—The pleura and peritoneum are usually normal, but sometimes show patches of pigmentation.

From post-mortem examinations on thirteen cases of malignant malaria in Macedonia GASKELL and MILLAR[1] divide fatal malarial infestations into three types—true cerebral, septicæmic, and cardiac. In the true cerebral there is an intense invasion of the brain by parasites. The numbers of parasites in the brain are disproportionate to those in the circulation, and the finding, in the capillaries and white matter of the brain, of forms intermediate between rings and crescents is taken as evidence that development progresses there. Treatment was useless. In the septicæmic form there was an extremely high parasitic content of the blood, followed by coma; treatment should be initiated on the detection of heavy hæmal infection, and before this has caused symptoms. The cardiac case is referred to on p. 234. See also Appendix VI—8, 9.

POST-MORTEM CHANGES IN THE THREE TYPES OF MALARIAL INFECTION

The pathological anatomy of the milder forms of malarial infection—benign tertian and quartan—can only be observed in cases where death is the result of some intercurrent malady, since these infections so rarely prove fatal. The literature of post-mortems in quartan cases is particularly scanty.

Acute benign tertian infection.—Death may be caused in rare cases by coma or hæmoglobinuria. There is pigmentation of the spleen, liver and bone-marrow. The spleen is enlarged; its blood shows a large number of parasites. The parasites in the fission stage tend to accumulate in the spleen. Spleen juice removed during life in the stage of invasion contains abundance of sporulating forms, which are scanty in the surface blood. The colon is sometimes inflamed. The endothelial cells in the cerebral vessels are swollen *and contain pigment. The urine in many cases contains casts.*

Chronic benign tertian infection.—*Spleen* enlarged and firm; contains parasites and pigment in the endothelial cells about the Malpighian bodies. Some hæmosiderin. *Liver* nothing macroscopical, but microscopically melanin is seen collected in large intracellular masses in the portal canal. The macrophages contain pigment. In one case (EWING) the patient was ill for twelve months, and died from endocarditis three months after the last malarial attack.

Quartan infection.—In quartan the enlarged spleen is not softened nor markedly melanotic. Similar absence of any conspicuous melanotic change in the liver and bone-marrow has been noted. Parasites may be found in the spleen and in the blood, but not in the brain. "The parasites are equally distributed in the various vascular areas of the body in all stages of their cycle. Splenic juice abstracted during the stage of invasion shows the same number of fission forms as is found in blood from the peripheral circulation."[2]

Acute malignant tertian infection—*macroscopical changes.*—The organ selected for sporulation suffers most, and produces symptoms giving the characters of that particular type of disease. The principal organs selected are—brain, intestine, heart, pancreas. *Body* pale yellowish in white races. *Heart* muscle pale and flabby; ecchymoses sometimes in epi- and endocardium. *Lungs* normal or congested. *Liver* enlarged, dark brown to slate colour on

[1] "Studies on Malignant Malaria in Macedonia," *Quart. Jl. Med.*, July, 1920, pp. 381–426. With text figs. Review in *Trop. Dis. Bull.*, Vol. 17, No. 2, February 14, 1921, p. 133

[2] MARCHIAFAVA and BIGNAMI's *Malaria* in *Twentieth-Century Practice of Medicine*, Vol. XIX, pp. 240, 241.

circulation. Even the smaller arterioles are sometimes found to be blocked by the infected red cells. Similar changes occur in the spinal cord.

Hæmorrhages of different kinds are often met with in cerebral pernicious attacks—they are usually punctiform and often numerous. These occur mostly in the white matter of the brain and cord, and in the strand of tissue between the white and grey matter (BIGNAMI). The writer has repeatedly found these punctiform hæmorrhages in the cortical substance of the brain.

The schizonts seen in the brain capillaries are near the stage of segmentation, many in the act of sporulation (Plate XIII, 131). In some cases every red cell is infected. The parasites do not (in malignant tertian fever) include crescents, which, curiously, appear post-mortem to be mainly contained in the rib marrow (W. M. JAMES),[1] bone-marrow generally and spleen. Free parasites, leucocytes, macrophages, endothelial cells containing melanin are also seen, as well as free pigment. The infected red cells adhere to the inner walls of the vessels and to one another, and form numerous small plugs.

"The nerve ganglion cells show signs of degeneration in their abnormal shape, disappearance of the chromatic bodies of Nissl, granulation of the protoplasm, and loss of chromatin in the nucleus" (S. P. JAMES).[2] This change may affect a large part of the brain, and is responsible for the headache, drowsiness and coma in children, and in acute malaria is a common cause of death. There is no blood clot, no fibrin is formed, and the leucocytes do not enter into the process; there is no thrombosis. In practice we know that in a large proportion of the cases, if treatment is adopted early and actively, the malignant symptoms pass off. The disappearance of severe coma under intravenous quinine is a revelation to those who see it for the first time.

Blocking by infected red cells and pigment in the cerebral arterioles and capillaries of various nerve centres explains at least some of the clinical manifestations of perniciousness—hyperpyrexia when the thermic centres are affected, aphasia when Broca's convolution is involved ; convulsions when the corpora striata are implicated, and so on for the other parts of the brain ; microscopic sections of brain in fatal cases have often shown these regional implications. The usual hypothesis is that some toxin exerts a special action on the walls of the small cerebral capillaries, giving rise to softening of the endothelial cells and causing the red cells to adhere to the capillary wall and block the capillaries. But against this is the fact that it does not occur in other organs in which the capillaries are small.

We may, however, have grave *clinical* cerebral malaria without any serious structural changes in the nerve tissues, cells and vessels of the brain, as may be inferred from the speedy recovery of a high percentage of these cases when properly treated with quinine from the beginning. This is a very common experience in military hospitals in India, where the cases are seen at once and treated promptly. In fatal cases of cerebral malaria without structural changes death is probably due to the effects of malarial toxins. Some authorities consider that obstruction of the blood vessels with parasites, pigment and altered endothelial cells is not met with in a large percentage of cases of cerebral malaria. They state that, were this the case, we should have it more frequently in benign tertian fever. Before segmentation many of the developed schizonts of benign tertian retire from the surface blood and pass through the vessels of the brain, although these parasites are comparatively large.

[1] *Proceedings of the International Conference on Health Problems in Tropical America*, 1924, pp. 68, 69.

[2] BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. II, p. 1577.

the hepatic cells show evidence that repair is proceeding. *Bone-marrow* usually pigmented and of a chocolate colour in the small bones, reddish in the long bones. The change in colour is due to replacement of the fat by vascular tissue.

E.—TREATMENT OF MALARIAL FEVER IN INDIA[1]

Once the diagnosis of malarial fever is complete, it is of paramount importance to see that the patient gets an effective dose of quinine, preferably by the mouth in solution. Other agencies may alleviate, but this is the only thing that can check the patient's paroxysms.[2] If the patient is in a serious condition from the malaria, and is unable to swallow or persistent vomiting is present, and a rapid action of the drug is required, it must be given either intramuscularly or intravenously. Quinine is *the* remedy in malaria. "In serious cases, to use any other drug to the exclusion of quinine is culpable trifling" (Sir PATRICK MANSON). With this the writer is in full agreement, provided "quinine" be used as a synonym for the crystallisable alkaloids of cinchona.

Rest in bed during any malarial fever is a very important auxiliary to the action of quinine. To attempt to "fight the fever" or walk it off is a great mistake, and is sometimes attended with serious risk, especially from complications. The drug is decidedly more efficacious in stopping paroxysms and destroying parasites when the patient is kept at a uniform temperature in bed to prevent chills, and properly nursed. During the cold stage keep the patient warm with blankets and hot bottles and hot, simple beverages; in the hot stage reduce the covering, give cold lemonade or iced water *ad lib.*, and, if the skin is dry, a dose of the ordinary hospital diaphoretic mixture every three hours, until sweating begins. After the sweating stage is over a change into dry clothing is called for. The food should consist of liquid, digestible nourishment, except in the milder attacks, when the patient may be given his ordinary diet. In serious cases, when the appetite returns a generous diet is to be allowed; the patient should have completely recovered before returning to work.

During the paroxysm of ordinary benign or quartan fever it is better not to give quinine until the sweating stage has set in and the temperature is falling. If a full dose of quinine in solution is given during the acme of the fever it may either be vomited promptly or set up nausea. When sweating has set in well give 10 grains of the hydrochloride (for choice) in solution, afterwards 10 grains *t.d.s.* after meals for eight or ten days; six doses of 5 grains each daily is preferred by some authorities.[3] Half a drachm of dilute hydrobromic acid aids solution and reduces ringing in the ears. Thereafter give 20 grains of a quinine salt daily for another week, subsequently 10 grains daily for two and a half months; or adopt one of the standard quinine treatments (pp. 272–276). If this is not done there will almost certainly be a recrudescence and one relapse after another, until a sort of relapse habit is established. A saline aperient weekly assists the quinine. In acute primary malaria small doses of quinine—10 grains twice a day—for four or five days cure about half of the cases permanently, assuming that re-infection is excluded. If there is anæmia give hæmoglobin in the form of red marrow, or a tablet of iron, arsenic and strychnine as a tonic, but continue the quinine as stated above. The anæmia is due to the malaria; if we eliminate the malaria by quinine the anæmia usually looks after itself.

[1] The subjects of QUININE IN MALARIA IN INDIA and ECONOMIC PROBLEMS CONNECTED WITH QUININE IN INDIA are dealt with in two special sections of PART III.

[2] The effects of the organic arsenical preparations are referred to later on.

[3] As a matter of fact it makes very little difference which salt of quinine is administered.

section; soft and congested. *Gall bladder* full of dark bile. *Spleen* enlarged, capsule tense; on section deep brown to black colour. *Stomach* and *intestines*, when affected, as in choleraic forms, show the mucous membrane congested, with blood-stained contents and flakes of mucus; dark pigmentation due to melanin, readily demonstrated by the microscope. *Lymphatic glands* swollen. *Pancreas* normal or in a condition of hæmorrhagic pancreatitis. *Suprarenal glands* congested. *Kidneys* normal or congested, with punctiform hæmorrhages in the pelvis and cloudy swelling in the parenchyma. *Bone-marrow* hyperæmic and chocolate-brown in colour. *Brain* normal or in the cerebral type shows œdema and hyperæmia of the leptomeninges; brown or black pigmentation of cortex and punctiform hæmorrhages in the white matter under the cortex. *Spinal cord* shows the same change as the brain. *Retina* may show hæmorrhages.

Microscopical changes.—Parasites found in the blood of heart, spleen, bone-marrow, capillaries of the brain, intestine, pancreas, etc., but the types are not differentiated clearly after death. They shrink considerably. The mononuclear cells show pigment granules. The polymorphonuclears show phagocytosis in a small degree. Macrophages may be seen from the internal organs containing parasites and red cells. *Heart* muscle loaded with hæmosiderin, and capillaries with parasites. *Lungs* contain parasites in all stages of development, with pigmented phagocytes and leucocytes. The pneumococcus is always present, and perhaps forms a double infection. *Liver*—the capillaries are enlarged and swollen by the endothelial cells loaded with pigment and filled with blood cells containing parasites and leucocytes with pigment. The perivascular lymphatics are swollen. The liver cells are compressed between dilated capillaries and contain hæmosiderin and bile pigment. Rarely there are localised patches of necrosis. Portal canals infiltrated with red cells containing parasites. *Spleen*—red cells show schizonts and crescents. Leucocytes and macrophages show pigment. *Kidneys* show pigmentation of capillary walls of glomeruli; parasites here are rare, but plentiful between the tubules, where phagocytes with pigment are also not uncommonly seen. The cells of the glomeruli show degeneration and shedding; the epithelial cells of the convoluted tubules show degeneration, and are cast off into the lumen. *Suprarenals* show irregular areas of vaso-dilatation, full of red cells, many of which contain parasites. The same may be said of the capillaries of the abdominal fat. *Bone-marrow* is chocolate-coloured in the small bones and brownish red in the long bones. It is soft and diffluent and contains sporulating parasites and crescents. *Brain* in cerebral cases has the capillaries full of sporulating parasites, large mononuclears, macrophages containing dead parasites. Nissl's bodies may be damaged and disappear, or show degeneration only. There may be degeneration of the neuro-fibrils. The punctiform hæmorrhages are due to the diapedesis of apparently normal cells.

Chronic malignant tertian infection.—Spleen, liver and bone-marrow are the parts always and chiefly affected. *Spleen* enlarged, firm, slaty, dependent upon the amount of contained pigment; signs of old perisplenitis, *e.g.* thickened capsule and adhesions; Malpighian bodies stand out boldly as they are enlarged and non-pigmented. Capillaries are dilated and are separated by splenic pulp or connective tissue containing giant cells. The pigment may be scattered diffusely, but is generally collected round the follicles, or extracellular and contained in lymphatics of arterioles or septa. *Liver* large, hard, pigment not always present, but seen at times gathered around the periphery of lobules; later the pigment is perivascular, and finally disappears. The capillaries or lymph spaces are dilated and by their pressure cause atrophy of the liver cells;

by constant blood examination that the parasites are eradicated; and the same remark applies to jails. But what has been said applies to a very large proportion of the cases treated as out-patients in our Indian civil hospitals.

It should be impressed on the patient that infestation may remain after all symptoms have vanished, showing itself in unexpected relapses, which constitute a peculiar danger to the very persons the carrier will be most anxious to shield, namely the members of his own family, or comrades, since an anopheline, after ovipositing, is apt to return to the spot where she obtained her original feed, and will in such a case have become infective.[1]

Warburg's tincture.—This is an old favourite that has been relegated to the limbo of forgetfulness in late years. It is an aromatic anodyne diaphoretic containing quinine, opium, aloes and various spices. It sometimes brings about a crisis in prolonged hot stages of paroxysms of the remittent or continuous types of sub-tertian fever when quinine given in the ordinary way for a few days seems to have no effect. It is not to be used as a substitute for quinine, but as an auxiliary to it. At one time it had a great reputation; in many a case it has tided the writer over difficulties, and even now, were he in practice in India, he would never be without it.

In the continuous quinine after-treatment the drug may be taken in uncoated tablets or tabloids, or in powder in rice wafers. Do not use sugar-coated tablets or tabloids without testing their solubility, because to prevent their becoming unsightly they require an impervious sub-coat. The writer does not trust quinine in pill form, except when *quite* freshly made up.

Salvarsan and its congeners in malaria.—Salvarsan and many of the organic preparations of arsenic have of late years been largely tried in malaria, either alone or in combination with quinine. When given intravenously or intramuscularly they do cause the parasites of benign tertian to disappear from the peripheral circulation. In some scientifically conducted experiments, such as those of Prof. J. W. W. STEPHENS in Liverpool, salvarsan removed benign tertian parasites from the surface blood more quickly than quinine. They do not seem to have any effect on malignant tertian and quartan parasites. Indeed, a number of deaths have resulted from the lighting up, by salvarsan given for syphilis, of a latent and unsuspected sub-tertian malaria. The beneficial effects of these remedies are limited to the period of the paroxysm, when fever and parasites are present; if given during the intervals in apyrexial periods they do not prevent relapses nor postpone them.

Stovarsol has been used with some success in the treatment of malaria. On *P. falciparum* it appears to have no action; to it *P. malariæ* has shown considerable resistance; following its administration *P. vivax* disappears from the cutaneous blood, but disinfestation seems to be exceptional. Of twenty-seven cases treated by intravenous injection of sodium stovarsol in an initial dose of 0·25 gramme (the daily quantity never exceeding 1·5 grammes and the total amount lying between 0·25 and 14·5 grammes) acute nephritis appeared in nine. A daily examination of the urine must be made and stovarsol replaced by quinine at the first sign of renal irritation, as it safely may.

Plasmoquine, or plasmochin, a German synthetic product, with affinities to quinine which are unknown or unstated, is a tasteless substance distributed in capsules of 0·05 gramme or in tablets of 0 02 gramme. The daily dosage advised, by mouth, is 0·08 or 0·1 gramme for three consecutive days, followed, after a four-days' interval, by a repetition of the course, this alternation being continued for

[1] C. C. BASS in *Southern Med. Jl.*, October, 1920, pp. 693–5; review in *Trop. Dis. Bull.*, February 14, 1921, p. 140.

Mild malignant tertian malaria is treated in the same way as simple tertian and quartan, but the patient must invariably be put to bed. Sub-tertian always calls for close watching, and the sooner the patient can be brought under the full influence of quinine, the sooner will there be a cessation of paroxysms, the less the chance of pernicious symptoms and relapse, and the less the degree of anaemia. Every case of malarial fever requires attention to the details of treatment. Attention to the general health, nutrition and habits does much to help the quinine. Want of due observance of details and inaccurate records have led to much of the present confusion regarding the precise position quinine should hold in the treatment of paroxysms and in the prevention of relapses. Remember that the findings in thin films are not always a reliable indication as to the intensity of the malarial infection—a single ring in a film may be all that is seen even in pernicious cases.

In all types of malarial fever, if there is persistent vomiting, cerebral symptoms, unconsciousness, hyperpyrexia, and when life is in danger from an overwhelming infection, quinine must be given intravenously—10 grains of the bihydrochloride in 20 c.c. of normal saline *secundum artem* (see pp. 264, 265). Pernicious cases brook no delay. The physician must know the nature of his case thoroughly if he is to save the patient's life. Microscopic examination of the blood in the vast majority of cases guides him as to what is to be done. If we see a case for the first time and find him suffering from an algid attack—blueness or greyness of the face and hands, low blood pressure, failing pulse, coma beginning—we do not think of standard treatments, *we know* that intravenous injection of quinine is the only thing that can save his life.

General remarks on quinine treatment of malarial fevers.—Without treatment by quinine, malarial fevers occurring in the inhabitants of malarial districts tend to become chronic; this is the ordinary course. Therefore the vast majority of the malarial infections in India (who may be considered never to take quinine) are chronic. The writer would again emphasise the fact that when malarial fevers are properly treated with quinine, the percentage of relapses, though often considerable, is smaller than when such treatment is not adopted. The absence of adequate quinine treatment causes a large number *of cases of infection by the more innocent parasites* to become chronic; it is well known that relapses of sub-tertian fever are readily prevented by the use of quinine, but some of the most serious forms of chronic malarial infection and malarial cachexia met with in malarial districts are due to benign tertian. Although when properly treated by quinine most cases of malaria do not relapse, the drug does often fail to eradicate all the parasites from the blood. It would appear as if quinine were in such cases incapable of attacking the parasites, perhaps ensconced in the vascular recesses of internal organs.

Chronic malarial infection most frequently occurs from the end of autumn onwards. When met with in the Indian Army the usual history of chronic malaria used to be as follows. The native soldier was brought to hospital for malarial fever in the late summer or early autumn, was placed under quinine treatment and discharged convalescent. He returned in a few weeks with fresh paroxysms, and this went on. So long as he was taking quinine the paroxysms were checked. This continued during the winter and often well into spring. He may or may not have been sent home on sick furlough more or less impregnated with malaria. At home he gradually got completely well, and may have remained so, or he suffered from a pernicious attack from which he may or may not have recovered. This is not the ordinary course of malarial infection at the present day, as most native soldiers are obliged to attend hospital regularly for their dose of quinine, until the medical officer is assured

plicating or debilitating conditions, such as ankylostomiasis, ascariasis, syphilis and malnutrition from whatever cause; such complications delay convalescence and may even prevent cure by quinine. Any attempt to eradicate malarial infection by the administration of quinine will be ineffectual without the assistance of the natural curative agents of the body. Complicating conditions must be concurrently treated, vital resistance increased and nature assisted in every possible way.

four to six weeks. Symptoms of poisoning are—lividity of lips, gums, tongue and nails, passing on to an ashen-grey skin, with collapse and hepatic pain. The blood is chocolate-coloured from methæmoglobinæmia; and a dark urine with a pale deposit, as appears in blackwater fever, has occurred after the taking of 0·6 gramme spread over eight days. Death has ensued. In seven of forty cases treated with daily doses exceeding 0·1 gramme lividity of the lips has appeared, an indication for cessation of administration. The immediate effect on schizonts of all three species of Plasmodium is satisfactory, although *P. falciparum* is the most refractory; nevertheless plasmoquine differs from all other known drugs in causing rapid disappearance of crescents from the cutaneous blood. Relapse has occurred in 31 per cent. of cases, the corresponding figure for quinine in like conditions being stated as 59. A combination tablet containing 0·125 gramme of quinine and 0·01 gramme of plasmoquine is recommended.

Mercurochrome-220 (dibromoxymercurifluorescein).—This remedy has recently been mentioned [1] in the treatment of malaria, but no details are as yet to hand. First introduced in 1919, it is now stated to be an internal disinfectant of high value. It is a synthetic dye, the number attached to it indicating its place in a series of disinfectants examined by YOUNG, WHITE and SWARTZ at the Brady Urological Institute, Baltimore. YOUNG [2] records successful results with it in the treatment of malaria, leprosy and anthrax. "It is given intravenously in 1 per cent. solution in doses up to 5 mg. per kilo weight of body." The author is not acquainted with this remedy, but considers that it should be tested clinically in India. All other substitutes for the alkaloids of cinchona bark are valueless in malaria.

Arsenical preparations.—Liquor arsenicalis is most useful as a blood restorative; the longer the series of paroxysms have gone on the better its effects. Liquor arsenicalis in fairly large doses (10 minims *t.d.s.* in adults) may be combined with the quinine in relapsing malaria with anæmia.

Arsenical preparations are sometimes reputed to cure malaria. They do so either by acting as general tonics, improving the blood-forming mechanism, or possibly in some cases by acting as anti-syphilitics. If there is much anæmia liquor arsenicalis may be given with or separately from the quinine. One of the best anti-malarial tonics used in Mesopotamia, on the North-West Frontier and in Afghanistan during the War was a tablet containing—arsenious acid $\frac{1}{80}$ grain, strych. sulph. $\frac{1}{80}$ grain, quinine 1 grain, reduced iron 1 grain, three times a day after meals. The writer cannot speak too highly of this combination in chronic malaria and malarial relapses. It has been definitely proved that in doses of 15 minims daily liquor arsenicalis fails to control the fever of malaria or cause the disappearance of parasites. In doses of 30 minims daily the temperature falls to the normal within 10 days, and in 13 out of 14 cases parasites disappeared in from 2 to 6 days.

Quack remedies in malaria.—There are at least half a dozen quack remedies sold extensively in India as panaceas for the cure of malaria and its complications. Thousands of people have faith in these preparations, and much money is spent on them. A certain class of the public accepts the brazen claims advertised. These advertisements usually denounce quinine as having many harmful effects on the body. The writer has subjected five of these preparations to the usual scientific tests; in none of them could he find any anti-malarial virtue whatever.

In order to give quinine full opportunity it is essential to remedy com-

[1] *Brit. Med. Journal*, November 27, 1926, p. 1004

[2] *Jl. Amer. Med. Assoc.*, 1926, 87, p. 1366.

PART III

METHODS OF PREVENTION OF MALARIA IN INDIA

communicating the disease from man to man by anophelines are reduced; quinine can effect this. In either of these two ways the chain of transmission of malaria could be broken.

A quarter of a century ago KOCH [1] and CELLI [2] recommended *wholesale cinchonisation of infected populations with a view to killing the parasite in the human host, thereby preventing mosquitoes from being infected.* ROSS,[3] in 1899, was the first to devise measures for an offensive campaign against the mosquito, and STEPHENS and CHRISTOPHERS,[4] in 1902, advocated segregation of the healthy in certain circumstances. Experience of the present century has taught us that practically every campaign against malaria should combine *defensive measures among susceptible persons and offensive measures against* parasites and their insect carriers.

TABLE OF METHODS OF PREVENTION OF MALARIA IN INDIA

The present-day methods of prevention of malaria are based on the principles enunciated above and may conveniently be included under the following *headings:*

Section 1 (*a*).—SEGREGATION OF THE HEALTHY IN INDIA.
(*b*).—ISOLATION OF THE INFECTED IN INDIA.
(*c*).—NOTIFICATION OF MALARIA IN INDIA.
(*d*).—ANTI-MALARIAL LEGISLATION IN INDIA.
2 (*a*).—QUININE IN MALARIA IN INDIA.
(*b*).—ECONOMIC PROBLEMS CONNECTED WITH QUININE IN INDIA.
3.—MOSQUITO CONTROL IN INDIA.
4.—PREVENTION OF MALARIA IN HUMAN HABITATIONS IN INDIA.
5.—MISCELLANEOUS AND ADMINISTRATIVE PROBLEMS CONNECTED WITH MALARIA IN INDIA.

SECTION 1 (*a*).—SEGREGATION OF THE HEALTHY IN INDIA

A comprehensive principle in the prevention of malaria is the keeping of healthy persons isolated from those that are infected with malaria parasites. This has reference specially to keeping away from Indian children the community we wish to protect.

J. W. W. STEPHENS and S. R. CHRISTOPHERS were the pioneers for segregation of the healthy, although this was empirically carried out in India for nearly a century by the erection of European troops' barracks at a distance from the local indigenous inhabitants. This is now generally carried out by Western nations that have colonial possessions in tropical climates. A zone of at least half a mile should separate the residential European quarters from the native town or quarter. Since such segregation has been introduced into West Africa a considerable improvement in the health of the European community has taken place.

The principle, of course, is the segregation of those who have the necessary knowledge, and the means and determination to carry it into effect, from those who are ignorant, apathetic or antagonistic in the matter. The former, as a

[1] *Report of the German Malaria Commission*, 1901.
[2] *Malaria*, p. 193.
[3] *Mosquito Brigades and How to Organise Them*, 1901.
[4] *Report to the Malaria Committee, Royal Society*, 1902.

PART III

METHODS OF PREVENTION OF MALARIA IN INDIA

General principles of prevention of malaria.—The general principles underlying the prevention of malaria are:

1. Malarial fevers are due to a species of protozoon which invades the blood of man.

2. This protozoon reaches the blood of man through some species of mosquitoes of the genus Anopheles.

3. In these mosquitoes malaria parasites carry out the sexual part of their life-history, undergoing developmental changes which are usually complete in from six to ten days, at the end of which time they reach the salivary glands of the mosquito, whence they are discharged once more into the blood of man.

4. These malaria-carrying mosquitoes breed chiefly in terrestrial waters in tropical and sub-tropical regions.[1]

To these may be added:

5. Quinine properly given cures the large majority of cases of malarial fever, and if taken regularly during the malaria season may prevent malarial paroxysms altogether.

About the foregoing statements there is now not the smallest shadow of doubt. They are scientifically established *data*. In the preceding and following pages is to be found an overwhelming mass of evidence which bears them out.

In the present state of our knowledge, therefore, it is reasonable to make three propositions:

1. Were all malaria-carrying anophelines exterminated or even greatly reduced malaria would cease;

2. Were all persons protected against the bites of anophelines no malarial infection could arise;

3. Were all existing cases of malarial infection cured malarial disease would be exterminated.

It is just possible that there is a gap in our knowledge, but for the practical anti-malarial sanitarian such a possible hiatus has to be ignored.

As corollaries to these three propositions we have the following:

(1) If anophelines can be diminished or prevented from attacking man, the chances of dissemination of malaria are reduced. The extermination of anophelines in India is not a practical proposition; their reduction is, and in anti-mosquito work it is better to concentrate effort on the reduction of those species known to act as carriers of human malaria parasites.

(2) If cases of malarial infection are lessened in number, the chances of

[1] Sir RONALD ROSS in ALLBUTT and ROLLESTON'S *System of Medicine*, Vol. II, Part II.

attack, and the poorer classes who have to work and live at all times without adequate protection are specially liable to be attacked. Again, even where they can be afforded, wire-gauze screens and mosquito nets get out of repair and permit of mosquito attacks. Nevertheless the principle of isolation from infected persons and from mosquitoes is sound, *and whenever practicable should* be carried out. (See pp. 51–54, THE HUMAN MALARIA-CARRIER.)

It is realised by many that it will take a few generations to raise the sanitary standard of the Indian multitude to a high level, and that it is folly for Europeans to dwell among them. On the other hand, some political, sociological and economic authorities are opposed to the principle involved on the ground *that it leaves the native to his fate. The writer considers that segregation of* the educated and healthy should be carried out until the ignorant and apathetic Indian is sufficiently educated in, and determined to avail himself of, anti-malarial sanitation. This principle is being violated by business concerns in various parts of the Indian Empire, where European employees live amidst coolie lines and swamps.

SECTION 1 (*b*).—ISOLATION OF THE INFECTED IN INDIA

As part of the general principles governing the prophylaxis of malaria, it is important that mosquitoes be prevented from biting infected persons. Isolation of those infected by malaria is to some extent now carried on in many of our hospitals in India, the patients being accommodated in mosquito-proof wards or provided with mosquito nets. This practice should be universal, not only for the acute but for the more dangerous convalescent stage. As a general preventive measure, however, isolation is, at present, impracticable. The children of the poorer classes, the most prolific source of malaria, cannot be isolated. Nevertheless, in spite of all these difficulties, the principle of isolation from mosquitoes should be adopted as far as practicable.

When carried out in their integrity, both segregation of the healthy and isolation of the infected as anti-malarial measures require careful and repeated examination of the blood of all persons concerned, remembering always that the blood of the infected may show no parasites, or may have them only during relapses, and that in ordinary circumstances persons may remain infected for years.

Malarial fever is a typically infectious fever, carried by anophelines, and all persons suffering therefrom are a source of danger to others and should be treated accordingly.

Segregation of the sick from the healthy requires large hospitals and hospital establishments, the use of mosquito nets or wire-gauze doors and windows, etc. The long-continued infective period of malaria renders legislation as regards compulsory notification and isolation impracticable. Where only a few cases occur, isolation is quite easy. By general protection from mosquito bites both methods (segregation of the healthy and isolation of the infected) are united.

Isolation is carried out as a routine measure in military life, and among our European troops; it is prolonged by sending the worst cases to non-malarial hill stations. During my last few years in India in the Army, we endeavoured to place malarial convalescents in separate mosquito-proof barracks until sexual forms of the parasite ceased to be shed into the peripheral circulation. The results were satisfactory.

rule, comprise Europeans and but a few of the native inhabitants of a malarial country. This segregation has its financial side, for the members of the former class are nearly always educated, specialised and expensive to replace, and should not be placed at the mercy of ignorance or fatalism. "For troops and officials segregation is always useful, and the detection and treatment of the sick must be urged whatever other methods are employed, because otherwise, even if local infection be absolutely abolished, a number of relapses will occur among old cases for some years to come."

If healthy persons in an infected area were absolutely protected from mosquito bites, fresh infection would not occur. Healthy residents outside the infected locality, and within the range of flight of infected mosquitoes coming from it, should also be completely protected from mosquito bites. The same applies to all persons coming to the locality, even for a single night. This measure is *segregation of the healthy.* Most of the malaria acquired by Europeans in India is got through anophelines that have been infected by Indians suffering from malarial fever. Personal servants of Europeans are often the source of malaria parasites. This is not always obvious, as the servant may have been ill some weeks previously and the incident may be forgotten. It must be remembered that the malaria parasite takes roughly ten days to develop in the mosquito, and another ten days to multiply sufficiently in the infected person, before malarial fever shows itself. Hence aside from any question of humanity, it is well to be on the watch for fever amongst servants, and to dose them properly with quinine when it manifests itself. In using quinine with servants one should always give it oneself, preferably in the liquid form. The mere putting of some quinine in a packet and telling him to take it at definite times is not sufficient. Often he has no faith in it, or he dislikes its taste or its effects, or is apathetic about such a minor trifle as ordinary *tap* or *bokhar*.

The method of segregation of the healthy is applicable to comparatively small bodies of men, such as garrisons in India, troops, gangs of labourers, jail prisoners, Government employees occupying isolated groups of buildings, and the supervising grades of many commercial undertakings.

For instance, it is desirable that bazaar people, and families with Indian children, should live remote from all troops and Europeans, seeing that in different malarious districts from 10 to 100 per cent. of children under ten years of age harbour malaria parasites in the blood when in apparent health, and have become infected in their homes. Troops in India, we know, often acquire malarial infection in the bazaars, in stations where there is a practical absence of anophelines in cantonments. Even for officers' quarters there are necessarily servants, frequently with their families, living in the compound with Anopheles in their rooms.

The segregation method can, of course, be applied by anyone who has the facilities for doing so. Indians who have the means, and wish to do so, may, equally with Europeans, isolate themselves from the infected population of malarious areas. There are numerous instances in which segregation can be carried out at comparatively little cost, especially when such radical measures as extensive and costly drainage schemes cannot be undertaken. For example, the removal of a few huts, or a bazaar, or even a village, on the confines of barracks or cantonments may make a marked alteration in the health of troops. Moving troops into tents, a fortnight or so after the rainy season has begun, and away from bazaars, is another method which may be successfully adopted in some stations.

Isolation from mosquitoes cannot, of course, in any sense be carried out in the plains. All have to work out of doors, often in places where anophelines

convinced the writer that over-legislation in sanitary matters is a mistake. The inadequate punishments awarded did not act as deterrents, whilst the loss of time involved in petty lawsuits for breaches of sanitary regulations was considerable. The actual working of a well-organised anti-malarial campaign should give very little bother to the people; its beneficial effects should lead to their co-operation, which is absolutely essential for success.

While it is useless to attempt to enforce a complicated legislation upon a people who are not educated up to a comprehension of the reason for the laws instituted, the anti-malarial sanitarian should have the support of the law in his undertakings. The following would appear to be some of the items upon which legislation is required.

Contractors, engineers and builders generally should be forbidden, under penalty, to interfere in any way with the course of natural drainage in their undertakings, and should be prohibited from creating borrow-pits. Where the latter are unavoidable they should invariably be filled up *before the work is relinquished.* All contractors should have a clause in their contract binding them to obey these regulations. Every line of railway and every highway hitherto constructed in India has been associated with the formation of borrow-pits, of which thousands of miles exist dispersed in all directions. These form one of the general breeding-places of anophelines. It would probably be impossible to fill these in now, but what can be done is to canalise roughly those that are actually in towns, cantonments and civil stations, and within half a mile of villages, and allow the waters to flow in the direction of the natural drainage.

Water in ponds, pools, basins, public or private places of resort or residence, or in depressions or excavations made for any purpose, should be covered with some protective netting, or drained off at least once a week, or should be covered with some form of petroleum sufficient in quantity to form a thin film over the entire surface once a week. Municipalities should have the power to treat all stagnant water with petroleum in such a manner as to destroy mosquitoes. For the method of procedure to be adopted in prosecutions see pp. 369, 370. Where there is no health officer or malaria officer the sanitary inspector should have power to prosecute offenders, in each case first obtaining the sanction of the municipal authorities to do so.

Water kept in cisterns, barrels, tanks, earthenware or other utensils for a period longer than one week should be protected from mosquitoes. Such water containers may be covered with wood, metal or wire gauze. Buckets containing water for longer than one week, such as fire buckets and other similar containers of stagnant water, should be covered in such a way as to prevent the entrance of mosquitoes, or emptied or treated regularly with petroleum. The chief anti-malarial sanitary law required for India is one that would lead to the *abolition of all stagnant surface water.* With well-thought-out anti-malarial sanitary legislation, and a proper public spirit, much could be done to lessen the malarial intensity of endemic malarial towns, stations and cantonments. The sanitary legislation of every province, town and cantonment should contain clauses placing among the list of nuisances all collections of water in which mosquitoes may breed, and giving power to all municipal boards and cantonment sanitary authorities to abate such nuisances. Most malarial countries have passed a series of anti-malarial legislative regulations and enactments, some of which date back a quarter of a century. In India the laws connected with anti-malarial measures should be united and systematised in a single enactment. The following Table of mortality from

SECTION 1 (*c*).—NOTIFICATION OF MALARIA IN INDIA

Notification as a general preventive measure of malaria in India is impracticable on account of the low standard of education of the people, and their unwillingness to consult qualified medical men for malaria. A large part of the population believes that disease arises from a visitation of some deity. Notification is, of course, to all intents and purposes in use in military garrisons, police battalions, jails, and a few other organised institutions, as all cases of malaria are soon brought under treatment in hospital or otherwise and precautions taken. In cities or towns where malaria has suddenly appeared or re-appeared it would be a useful auxiliary in the hands of public health authorities. It has been practised in the United States of America for some years, and was adopted in England in 1916. It cannot be recommended for large endemic districts in India; no staff exists to carry it out. It is quite feasible in hill stations.

In an intensive anti-malarial campaign in any localised area, notification should form an integral part of the operations. Any trained M.O.H. is able to draw up a suitable scheme for introducing "notification of malaria."

During the Great War, when large numbers of troops were returning to the United Kingdom heavily infected with malaria acquired at various fronts, and an epidemic of the disease threatened, notification of malaria was, as just noted, adopted in England under Section V of the Local Government (Emergency Provisions) Act of 1916 and the Public Health Regulations, 1919. It is only necessary to refer briefly to the former.

Notification of malaria.—Article V states: "Subject to the provisions of these regulations and subject to the provisions of Section V of the Local Government Act *mentioned, every medical practitioner, as soon as he becomes* aware that a person upon whom he is in professional attendance is suffering from malaria . . . shall forthwith make and sign and send or deliver a notification of the case containing the particulars to the M.O.H. for the District; provided that the case has not been notified during the preceding six months." On receipt of this intimation the M.O.H. has his specific duties to discharge.

Article X states: "In every case of malaria occurring in his District, of which the M.O.H. becomes aware, and in which he considers that action is necessary to prevent the spread of infection, he shall take all practical steps to ensure that the person suffering from malaria—

(1) Is supplied with efficient mosquito netting.

(2) Receives necessary quinine treatment.

(3) Receives proper advice as to continuation of quinine treatment in order to prevent relapses; and

(4) Receives proper advice as to the precautions to be taken to prevent the spread of infection."

The Notification Act under reference is still in operation. As the result of rigid observance of these emergency laws initial malaria has been once more practically eradicated from England.

SECTION 1 (*d*).—ANTI-MALARIAL LEGISLATION IN INDIA

A superfluity of sanitary legislation in India tends to defeat its own ends, and ten years' personal experience as health officer of a large municipality

The literature in connexion with the introduction of cinchona cultivation into India is vast. For the information on the subject contained in this and the next sections the writer is mainly indebted to three highly interesting volumes—Sir GEORGE KING'S *Manual of Cinchona Cultivation in India* (Calcutta, 1876); Sir CLEMENTS R. MARKHAM'S *Peruvian Bark: A Popular Account of the Introduction of Chinchona Cultivation into British India* (1860–1880); and JOHN ELIOT HOWARD'S *Quinology of the East Indian Plantations*, Parts I, II and III (1876). Many parts of India and Burma were explored to obtain suitable sites having the required altitude, rainfall and soil for the different species of the plant. The Dodabetta plantation in Ootacamund (7,500 to 8,000 feet) grows chiefly *C. officinalis* and *C. pilayensis* and some hybrids, the Paikara plantation (5,000 to 6,200 feet and 10 miles from Ootacamund) grows *C. succirubra*, *C. officinalis* and *C. micrantha*. Nedirattam plantation (from under 5,000 to 6,000 feet, 16 miles from Ootacamund) grows *C. succirubra*,[1] *C. calisaya*, *C. micrantha* and the delicate species *C. peruviana*. The Sikkim plantations (old and new) are in the valley of the Rangbi, 12 miles from Darjeeling, at elevations ranging from 4,400 to 6,000 feet; the rainfall is 150 inches. They form an irregular belt at the bottom of the valley, and extend upwards along the slopes of the hills around. The Rangbi Valley is shut in upon all sides, and is protected from wind up to the whole limits of the cinchona zone; at the lower limits frosts do not occur. Mungpo is on a spur running eastwards, the direction in which all the later expansions have taken place. The chief species of cinchona grown are—*C. officinalis*, *C. calisaya*, the hybrid *C. succirubra*+*C. ledgeriana* and *C. micrantha*. In Burma the Thandoungyee plantation (3,700 to 4,400 feet), 18 miles north-east of Toungboo, in the Karen Hills, grows *C. succirubra* for the production of cinchona febrifuge for the province.

Almost every range of hills from 2,500 to 9,000 feet in height has been explored for sites for cinchona plantations, and many have been experimented with, such as the Palnais, Shevaroys, Wainad Plateau, the mountainous region of Coorg, the Mahbleshwars, the Khassia and Jantia Hills (Assam), Dehra Dun, Garhwal, and the Kangra Valley. For one reason or another all have been abandoned.

The total yield and the relative proportions of the different alkaloids differ in each species. Many experiments in grafting and cross fertilisation have been made. In grafting, the grafts retain their respective alkaloids in the natural proportion, just as if growing separately. Hybridisation is also uncertain, hence the method of propagating the best varieties by cuttings has been adopted, except in the case of those that do not strike readily, such as *C. ledgeriana*, in which the plants are grown from the shoots of felled trees. If the bark is removed from the trunks in alternate strips, so as not to injure the cambium, a new layer of bark is formed in one year which is richer in quinine than the original bark and equal in thickness to that of two or three years' ordinary growth. This is the "renewed bark" of commerce. This method of stripping is now begun when the trees are eight years old, at which age the bark separates most easily. The yield of quinine increases annually until the eleventh year, at which age it seems to reach its maximum.

The alkaloids are contained in the cellular tissue of the phloem.[2] No definite knowledge has as yet been obtained of the exact steps by which they are formed in nature in the tissues of the bark. Quinine is present in only small quantities

[1] The zone of the "red bark" is from 2,450 to 5,000 feet.

[2] JOHN ELIOT HOWARD, F.R.S., *Quinology of the East Indian Plantations*. The world is for all time indebted to the genius of this great chemist for his work on cinchona plants and the chemistry of their various alkaloids.

malarial fevers in Italy before and after anti-malarial legislation was introduced is interesting and instructive.

Years.	Mortality figures	Proportion of deaths from malaria per million inhabitants.	Remarks.
1888 . .	15,987	536	
1902 . .	9,908	302	Application of laws against malaria, and commencement of general use of quinine in endemic malarious areas.
1903 . .	8,511	258	
1908 . .	3,477	102	

An Anti-Mosquito By-law suitable for municipalities is given in Appendix III.

SECTION 2 (*a*).—QUININE[1] IN MALARIA IN INDIA

A brief account of the introduction of cinchona bark into European therapeutics and of its early use in India is given in the HISTORY OF MALARIA (pp. 1–4). The ECONOMIC PROBLEMS CONNECTED WITH QUININE IN INDIA are dealt with *in extenso* at the end of this section.

The cinchona plant.—*Cinchona* belongs to the Natural Order Rubiaceæ, and includes trees of varying size up to 80 feet, with evergreen leaves and deciduous stipules. "The flowers are arranged in panicles, white or pinkish in colour, with a pleasant odour, the calyx being 5-toothed and superior, and the corolla tubular, 5-lobed and fringed at the margin. The stamens are 5, almost concealed by the corolla, and the ovary terminates in a fleshy disk. The fruit is an ovoid or sub-cylindrical capsule, splitting from the base and held together by the apex. The numerous seeds are flat and winged all round "[2] (Plate XV) There are about forty species described, but only a dozen or so have been used commercially. They are indigenous in the western mountainous regions of S. America, flourishing generally at from 8,000 to 9,000 feet, but some species have been found as high as 11,000 feet, and others as low as 2,600 feet.

The trees are valued entirely for their bark, which contains the most potent remedies against malaria ever discovered, *viz.* the cinchona alkaloids. Obtaining the bark in its natural habitats in New Granada, Ecuador, Peru and Bolivia is a work of immense labour and hardship. The trees grow isolated or in small clumps in dense forest, which has to be cut to reach them, and then they have to be freed from twining plants and parasites. The Indian then beats and cuts the stem bark as high up as he can reach. Next the tree is felled and the whole bark of the stem and branches secured. The bark of the smaller branches, as it dries, curls up, forming "quills," the thicker bark of the stems forming the "flat" bark of commerce. The destructive methods of collecting bark were steadily diminishing the natural sources of supply, and this led to the successful transplantation of several species of cinchona in various countries, especially India and Java. India owes a great debt of gratitude to Sir CLEMENTS R. MARKHAM, who brought young trees originally from S. America and planted them in the Nilgiris, and to Dr. FORBES ROYLE, who for many years had pressed upon the East India Company the urgent necessity of introducing cinchona cultivation into India. Also to Dr. T. ANDERSON and Lt.-Col. Sir GEORGE KING, I.M.S., who tended the cinchona plantations at Mungpo in the Rangbi Valley, Sikkim, during their infancy, brought them to maturity and perfected the industry of extracting the alkaloids from the bark. At the present time cinchona is grown in the Nilgiris, Ceylon, and in the Karen Hills of Burma, as well as in Sikkim.

[1] The word *quinine* is used throughout this volume either in a general sense to signify the products of cinchona bark, or with reference to sulphate of quinine, the most commonly used and cheapest salt of the alkaloid *quinina*.

[2] *Encycl. Brit.*, 11th Ed., Vol. VI, p. 369.

artificial quinine will be synthetically prepared, equal, if not superior to, the natural alkaloids in malaria. Many derivatives can now be made by replacing some of the groups attached to the molecule by others; so far only a few such derivatives have been prepared and used successfully in malaria. Euquinine is one of them, plasmoquine perhaps another. Doubtless others will be discovered. This work will be slow. The chemical and physical difficulties in these investigations are numerous.

Adulteration of quinine salts and cinchona febrifuge is very profitable and not uncommon, especially during periods of epidemic malaria and war (see pp. 279, 280). The chief impurities met with are starch, flour, carbonate of magnesia, chalk and an excess of moisture in quinine sulphate.

In modern times a large number of substitutes for quinine have been introduced, some of which have been administered empirically, others because it is considered that from their effect on other animal parasitic forms they should bring about the destruction of malaria parasites. In no single instance can these substitutes compare in efficacy with quinine.

The most recent observations indicate that quinine and its allies are *facile princeps* the best remedies in malarial fevers. This position, claimed for quinine by Sir PATRICK MANSON a generation ago, remains unassailable to-day. Its high reputation in malarial therapeutics has been established by a century's practical experience. Tropical and sub-tropical countries would be in a sad way without quinine. To emphasise this we have only to recall the harrowing picture of an Indian village in an endemic malarious district with most of its inhabitants impregnated with untreated malaria, and in which the survivors with chronic malaria and malarial cachexia are going through the slow process of natural immunisation. On the other hand, we should remember that there are whole districts of endemic malaria in India, especially some hill regions, where there is little obvious deterioration of health from malaria, just as there are districts where hookworm disease causes serious anæmia, etc., and others in which the people with hundreds or even thousands of the worms seem to suffer no ill effects from them. There is seemingly an unknown factor at work in some cases.

In extolling quinine and its allies as *par excellence* the drugs in malaria it is not meant that they are sovereign remedies or perfect specifics in the group of malarial diseases. Quinine has its limitations, and it is the non-recognition of this fact that has led to its decline in popularity and the introduction of numerous substitutes in recent years. Prof. W. E. DIXON, F.R.S., in his address at the Annual Meeting of the British Medical Association, 1920, stated: "What is required is not super-quinine, but a quinine with more specialised elective action on certain organisms. Iso-amyl hydrocupreine is from ten to twenty times more powerful than quinine (1) in destruction of protozoa; (2) as a germicide; (3) as a local anæsthetic." He stated that of this preparation 25 grains can be administered in the twenty-four hours without harm. Lastly, he remarked that observations made during the last few years show that we are only touching the fringe of the pharmacology relating to the quinine derivatives.

Quinine salts should be up to standard strength in the alkaloid quinina.—It is important that the salts of quinine, whether used curatively or prophylactically, should be up to the standard in the alkaloid *quinina* laid down in the British Pharmacopœia. Further, the writer would urge that all approved alkaloids of cinchona bark, and their salts and cinchona febrifuge [1]

[1] It will be difficult to fix a standard for the mixed cinchona alkaloids, but it is possible if some elasticity is allowed in the proportions of the various alkaloids. FLETCHER'S suggestion to meet this difficulty is noted below.

in the leaves, but in larger quantity in the stem bark, increasing as the root is approached.

The altitude at which the trees are grown seems to affect the production of quinine, *e.g. C. officinalis* produces more quinine above 6,000 feet than below that elevation, and at the same time quinidine, cinchonidine and resin are increased. Some barks yield no quinine below 6,000 feet, but produce a fair quantity at 7,500 feet. Free access of air appears to affect the yield of quinine —"renewed bark" contains, as noted, more quinine than the original bark.

The alkaloids exist in the bark chiefly in combination with cinchotannic and quinic acids. The former is seemingly changed by oxidation on exposure into a red colouring matter (cinchona red), which is very abundant in some species, as in *C. succirubra*. For this reason the barks which contain little colouring matter (*C. calisaya, C. ledgeriana* and *C. officinalis*) are preferred, the quinine being more easily extracted from them in a colourless form. The method of extraction of quinine and other alkaloids by private manufacturers is a secret.

Red cinchona bark is obtained from the stem and branches of *C. succirubra*; a large proportion of that used in the Indian factories comes from Java. It should not yield less than 5 per cent. of the alkaloids of cinchona. The bark occurs in quills or more or less incurved pieces of varying size, often about 35 millimetres in diameter, the bark itself being from 2·5 to 6 millimetres in thickness. The outer surface is dull brownish grey or reddish brown in colour, often grey with lichens, and more or less strongly wrinkled longitudinally, older pieces also bearing reddish warts; small transverse cracks are sometimes seen. The characteristic red-brown inner surface shows on scraping a yellowish brown interior, which darkens on exposure. The bark is spongy in texture, and has no perceptible odour, but a distinctly bitter and astringent taste. It should not yield more than 5 per cent. of ash on incineration. Other quilled barks appearing in commerce are those of *C. calisaya, C. officinalis, C. lancifolia* and *C. ledgeriana*. Calisaya bark or yellow cinchona occurs in firm hard quills, the periderm of which is liable to exfoliate, and bears well-marked longitudinal and transverse cracks. It contains about 6 per cent. of alkaloids, of which about one-half to three-quarters is quinine. Ledger bark closely resembles calisaya, but is marked with more numerous and less conspicuous long fissures and transverse cracks. It yields from 6 to 10 per cent. of total alkaloids, and from 3 to 8 per cent. of quinine.[1]

Imported cinchona bark is never uniform in quality. That from S. America contains a variable admixture with inferior barks. The Indian barks comprise, under the names of yellow, pale and red barks, a number of varieties of unequal value.

PHARMACOLOGY OF CINCHONA ALKALOIDS

General remarks.—We have still much to learn regarding the chemistry and pharmacology of the different alkaloids and derivatives of cinchona bark; also regarding their absorption, metabolism, method of excretion from the body and their action on malaria parasites. It is not until these points are settled that we will be in a position to express definite and reliable opinions on many of the questions relating to the administration of quinine in the cure and prevention of malarial infections. The extreme complexity of the chemical constitution of the alkaloids and derivatives has only become fully recognised during the last decade. It is possible that when the actual chemical constitution of the various molecules of the alkaloids has been worked out some form of

[1] Abstracted from *British Pharmaceutical Codex*, 1923.

in favour of the alkali. The question may, therefore, be considered to be still *sub judice*.

Quinine bisulphate contains 59·1 per cent. of the alkaloid, is soluble in 11 parts of water, and 1·24 parts of it contain as much quinine base as 1 part of quinine sulphate. It is administered like the sulphate.

Quinine hydrochloride, $C_{20}H_{24}N_2O_2 \cdot HCl \cdot 2H_2O$.—This salt resembles the sulphate in appearance; the crystals, however, are somewhat larger. It contains 81·8 per cent. of the alkaloid, is soluble in 40 parts of water, and 0·9 part of it contains as much quinine as 1 part of quinine sulphate. It is, perhaps, the most valued salt of quinine for oral administration, and where the question of expense does not come in it is the one recommended. It is given in the same way as the sulphate, and is sometimes used for intramuscular injection. This salt circulates in the alkaline blood without precipitation, probably owing to the presence of carbonic acid in the blood. The doses are smaller than the sulphate owing to its greater solubility and greater quinine content.

Quinine bihydrochloride, $C_{20}H_{24}N_2O_2 \cdot 2HCl \cdot 3H_2O$.—Occurs in a colourless crystalline powder. Contains 72 per cent. of the alkaloid, is soluble in 1 part of water, and 1·02 parts contain as much quinine base as 1 part of the sulphate. It is the most soluble salt of quinine, and is said to be the one most rapidly and completely absorbed. When it is desired to use a salt of quinine as a tonic, this is the best one to employ. It is administered like the sulphate; it and the bihydrobromide are extensively used for intramuscular and intravenous injections.

Quinine hydrobromide.—Contains 76·6 per cent. of the alkaloid, is soluble in 45 parts of water, and 0·96 grain of it contains as much quinine base as does 1 grain of the sulphate. It is administered in the same way as the hydrochloride. It and the following salt are useful when quinine sulphate produces headache, unusual deafness or ringing in the ears, or where there is a special idiosyncrasy for quinine. Ten grains contain as much bromide as 3 grains of bromide of potassium.

Quinine bihydrobromide.—Contains 60 per cent. of the alkaloid, is soluble in 7 parts of water, and 1·23 grains contain as much quinine base as 1 grain of sulphate. It is used in the same way as the bihydrochloride.

Cinchona febrifuge (mixed cinchona alkaloids).—This originally was a combination of all the alkaloids and active principles extracted from *Cinchona succirubra* bark. As now made in Mungpo (Sikkim) it consists of the *residual alkaloids* after the quinine has been extracted from different species of bark, a certain percentage of quinine being added so as to make a preparation similar to the original cinchona febrifuge in composition (p. 297). As met with generally, it appears to consist of any mixture of the bark extracts and by-products of quinine manufacture which the makers wish to sell. Some of these mixtures are of excellent quality and contain a large amount of the alkaloids, and are considered by many experienced physicians to be therapeutically as good as quinine; others are decidedly inferior, if not quite useless, because they contain little or none of the alkaloids.

Cinchona febrifuge may be administered in mixture, tablets, fresh pills, or in gelatine capsules. If given in mixture it should be thoroughly strained, otherwise it may become slimy, the amorphous alkaloids sticking to the mouth and tending to produce nausea. It is best given as uncoated tablets. In this form it is a satisfactory and valuable substitute for quinine sulphate. The alkaloids are found in the urine in 105 minutes after five 4-grain tablets are swallowed; if taken in solution the alkaloidal reaction (p. 280) appears in one-third of the time. It is said to be equivalent in value to the same quantity of quinine

(mixed cinchona alkaloids), should be made officinal and the strength of their salts in the alkaloids fixed legally in the British and Indian Pharmacopœias.

Cinchona bark contains no fewer than fourteen known alkaloids. Of these the more important in malaria are quinine, cinchonine, cinchonidine and quinidine, all crystallisable. Quinoidine is the mixture of the uncrystallisable or amorphous alkaloids remaining after the crystallisable alkaloids have been removed from the extract obtained from the bark. Up to date quinine is the only officinal alkaloid, and its salts have been in greatest favour in the treatment of malaria.

Quinine, $C_{20}H_{21}N_2O_2$, is isomeric with quinidine, but is lævo-rotatory. It yields an emerald-green colour with chlorine water and ammonia. The quantity in different species of bark varies considerably.

Cinchonine, $C_{19}H_{22}N_2O$, occurs in colourless prisms, is dextro-rotatory, and unlike quinine and quinidine does not yield a green colour with chlorine water and ammonia.

Cinchonidine, $C_{19}H_{22}N_2O$, is isomeric with cinchonine, is lævo-rotatory, slightly soluble in ether and fluorescent.

Quinidine, $C_{20}H_{24}N_2O_2$, is isomeric with quinine, from which it differs in crystallising in prisms instead of needles, in being dextro-rotatory and not lævo-rotatory, and in being insoluble in ammonia except in excess.

The official salts of the alkaloid quinina are—the sulphate, hydrochloride (formerly called hydrochlorate) and bi-(or acid-)hydrochloride, in addition to which other quinine salts are widely used, *viz.* the bisulphate, hydrobromide and bihydrobromide.

Quinine sulphate, $C_{20}H_{24}N_2O_2,H_2SO_4,H_2O$.—This is the neutral sulphate. It occurs in very slender acicular crystals, contains 73·5 per cent. of the basic alkaloid, and is soluble in 800 parts of water. It is precipitated from its solutions by alkalis and carbonates, but is very soluble in ammonia. The acid solution is fluorescent. When a solution of chlorine is added, followed by ammonia, an emerald-green colour, due to the formation of thalleoquin, is developed; a 1 in 5,000 quinine solution is detected by this test, and if bromine is used instead of chlorine, one of 1 in 20,000. The fluorescence is visible in the acid solution of 1 in 200,000. Owing to its voluminous character 18 per cent. of water may remain in apparently dry samples of quinine sulphate. If it loses more than 14·6 per cent. of water when dried at 100° C., water is in excess.

This salt is the standard by which the salts of the other alkaloids and cinchona febrifuge are compared in malaria. It is the cheapest and most generally used salt of quinine, and is manufactured on a large scale by the Government quinine factories. It is best given in an acid solution (1 minim dilute sulphuric acid or 1 grain citric acid to each grain of quinine sulphate), but it may also be administered as powders, tablets, tabloids, cachets, capsules and freshly made pills.

The sulphate is good for continuous use. It is less liable to cinchonise than the more soluble salts, and possibly its slower absorption secures a larger quantity and less variability in the amount in the circulation, and a more continuous action. ACTON and KNOWLES [1] demonstrated that quinine was more lethal to Paramœcium in the presence of an alkali. Acting on this, Major J. A. SINTON, V.C., I.M.S., used an alkaline mixture of bicarbonate and citrate of sodium separately from a quinine mixture in the treatment of cases of malaria, with satisfactory results. The latest critical tests, however, are not strikingly

[1] "Results of some Experiments in the Treatment of Malaria with Alkali Combined with Quinine," *Ind. Jl. Med. Res.* of 1923, pp. 850–6.

the surface blood, and fever, quite as rapidly as did quinine. On this and other reports obtained at the instigation of the Medical Research Council it is concluded that quinidine is as efficacious as, and no more toxic than, quinine, and that there is no evidence of preferential action of quinine on sub-tertian, and quinidine on benign tertian, infections.

Cinchonidine sulphate.—Fletcher's results with this salt were closely parallel to those with cinchonine sulphate.

The result of these and other investigations is that, in two 10-grain doses daily for adult males, all these alkaloids are equally valuable, that in smaller quantities quinine and quinidine are superior. "The real importance of the conclusion reached is that it deposes quinine from the position of unique value which practice and tradition have accorded to it among the cinchona alkaloids." The Committee of Medical Research Council is continuing work on the other alkaloids. If further investigation establishes the curative and toxic qualities of these crystallisable alkaloids as being generally equal, the question of their mixture in a "cinchona febrifuge" would greatly cheapen malarial treatment in India.

Cinchonine is declared by some authorities to be of equal value to quinine in malaria, others consider it to be poisonous. MacGilchrist[1] holds the former view, Acton[2] the latter. These discordant results were in all probability due to impurities in the drugs used by different observers. When guaranteed pure cinchonine has been used, the results have been uniform and satisfactory. The latest result recorded is summed up by Dr. W. Fletcher[3] (1925) from the Kuala Lumpur work on behalf of the Medical Research Council as follows:

"(1) Cinchonine in doses of 0·1 grain per kilo of body weight is less efficacious than quinine in reducing the fever and in clearing malaria parasites from the peripheral blood.

"(2) Cinchonine in doses of 0·1 grain per pound weight of body is as effective as quinine.

"(3) Cinchonine is not more toxic than quinine."

Notwithstanding all that has been written about the different effects of the above-named alkaloids of cinchona bark in malaria and their selective action on simple tertian and malignant tertian parasites, the writer believes that there is very little to choose between them.

Quinoidine (combined amorphous alkaloids of cinchona bark).—A. C. MacGilchrist[4] (1915), W. H. Acton[5] (1920) and W. Fletcher[6] (1923) found quinoidine to be too poisonous to use in malaria; Sir David Prain[7] (1924) and E. Waters[8] (1916) found it to be as effective in malaria as quinine, and non-toxic. "The only explanation of this discrepancy, which occurs to us, is that the quinoidine used by MacGilchrist, Acton and ourselves was a different substance from the drug used by Waters and Prain. Possibly the modern methods employed in extracting alkaloids from the bark with hot mineral oil have rendered the non-crystallisable residue less efficient and more toxic than it was when the extraction was carried out with acidulated water."[9] Fletcher found that quinoidine had no appreciable action on malaria para-

[1] *Ind. Jl. Med. Res*, 1916, ii, p. 45.
[2] *The Lancet*, 1920, i, p. 1260.
[3] *Bull. Inst. Med Res., Federated Malay States*, No. 3 of 1925.
[4] *Ind. Jl. Med. Res.*, 1915, ii, p. 889.
[5] *The Lancet*, 1920, i, p 1260.
[6] *Notes on the Treatment of Malaria with the Alkaloids of Cinchona*, 1923, pp. 18, 19.
[7] *Brit. Med. Jour.*, 1924, i, p. 1023.
[8] *Ind Med Gaz.*, 1916, ii, p. 335.
[9] Dr. William Fletcher, *Further Notes on the Treatment of Malaria with Cinchona Febrifuge, Quinidine and Cinchonine* (1925), p 9.

sulphate in the treatment of malaria; whether it is really so is a matter of vast economic importance to India, as its manufacture is much less costly than that of the sulphate of quinine. It is made in the Government factory at Mungpo (Sikkim), and also in Java.[1]

The average analyses of Indian and Javan cinchona febrifuge and of Indian residual alkaloids—MacGilchrist, 1916, and W. Fletcher,[2] 1923—are given below:

	Cinchona febrifuge.		Residual alkaloid.
	Indian.	Javan.	Indian.
	per cent.	per cent.	per cent.
Quinine	7·4	11·5	3
Cinchonine	18·58	26·3	35
Quinidine	22·83	5·0	20
Cinchonidine	5·81	20·0	2
Quinoidine	29·12	37·2	30
Water and ash	16·23		10

Cinchona febrifuge has no fixed pharmaceutical composition—different samples vary considerably (see p. 297), and are often subjected to sophistication. The drug is issued from the Government quinine factories in powder and tablets.

It is of paramount significance that the Indian cinchona febrifuge of to-day is not the total cinchona alkaloids, but a residual alkaloidal preparation. The price of both Indian and Javan cinchona febrifuge is considerably lower than that of quinine sulphate. Any return to the use of cinchona febrifuge on a large scale demands a full consideration of the risk of adulteration associated with the use of an unstandardised drug and the urgent need of establishing a standard for that preparation as early as possible.

Dr. William Fletcher[3] has lately completed a very important series of investigations regarding the relative value of cinchona febrifuge and quinine in the treatment of malaria. In strictly controlled tests it was found that in dosages of 0·1 grain per kilo of body weight, quinine was more satisfactory than cinchona febrifuge. When the dosage was 0·1 grain per pound both were equally effective. Larger dosages of febrifuge were unnecessarily toxic, the presumed result of a high percentage in the sample of amorphous alkaloid, and not more effective. "Cinchona febrifuge is, therefore, to be looked upon as an inexpensive method of treating the disease, but owing to the varying composition and length of time required for making a difficult analysis (ten days) for legal control it is proposed that the Government of Malay should purchase the production in bulk, have it assayed, put up in tablets and issued authoritatively. It could thus be used of standard composition for the majority of the people, while quinine could still be employed by those able to afford it."[4]

Quinidine sulphate.—In strictly controlled tests in which each patient received 0·1 grain per kilo of body weight of quinine and of quinidine sulphate twice daily, William Fletcher found that the latter removed parasites from

[1] The question of supplementing sulphate of quinine by mixed cinchona alkaloids in the treatment of malaria is dealt with *in extenso* in the section on Economic Problems Connected with Quinine in India, pp. 290–200.

[2] *Annual Report of the Institute of Medical Research, Federated Malay States, for the year* 1924.

[3] *Bull. Inst. Med. Res., Federated Malay States*, No. 3 of 1925.

[4] Editorial in *Brit. Med. Jl.*, January 23, 1926, p. 154.

threatening to overwhelm the system 25 per cent. in excess of the quantities named should be given. In children, if pernicious symptoms exist, give full doses, and in the same circumstances in adults use the bihydrochloride or bi-hydrobromide intravenously. Children require more quinine relative to their body weight than adults; they should be kept in bed throughout; it is specially necessary to watch the effects of the quinine on the temperature and on the parasites, being guided by these effects in regard to the quantity of the drug to be given; the larger doses should be stopped when the peripheral blood is free from parasites. For all ages large doses should be avoided in ordinary cases; they do not give as good results as moderate doses. It will seldom be necessary in adults to exceed 30 grains a day given in two or three doses. Prophylactically the drug is given in one of the ways detailed on p. 283.

There is much evidence to support the view that there is an optimum daily quantity of quinine during the curative period, that is, the period of *immediate cure* (p. 279); that this quantity is not the same in different persons, and that possibly this dose varies in the same person at different times.

Methods of administration.—Quinine may be given by the mouth, intramuscularly, intravenously or *per rectum*. It should never be administered hypodermically in India. There is little difference in the relative success of the various methods of giving quinine in *ordinary* cases.

By the mouth.—Oral administration is, and must remain, the ordinary method of administering quinine. It is given by the mouth in solution, powder, tabloids or tablets, capsules, cachets, or pills. The majority of medical practitioners in India consider that the most satisfactory way of giving quinine to produce the maximum effect in malaria is in solution by the mouth. Until recent years, throughout the Indian Army and in jails quinine was given in solution, both when used curatively and prophylactically. The use of tablets of quinine has now largely taken the place of the mixture.

The ordinary quinine mixture consists of 5 grains of the sulphate with 5 or 10 minims of dilute sulphuric acid, and an ounce of water or chloroform water. Both the hydrochloride and bisulphate are preferred by many doctors, and are largely used where the question of cost does not arise; if it does, then the sulphate is used—it is cheaper and it is made in India. There is, however, no evidence that the more soluble salts give better results than the sulphate; the writer believes that solubility has nothing to do with the anti-malarial effects. When 10 or 15 grains are to be given, 2 or 3 ounces of the mixture mentioned are administered—this is preferable to giving the larger doses in an ounce of water. It is best taken, and has fewer disagreeable after-effects, just before a meal—the first mouthful of food removes the bitterness. Some flavouring agent may be added to the mixture. If it disturbs the heart's action 5 minims of tincture of strophanthus or digitalis may be added, or a few grains of citrate of caffeine taken with it. In whatever form quinine is used, it is better to adhere to a uniform method of administration. Quinine is given in the form of powder by the mouth with the object of avoiding the bitterness of the mixture. Ordinarily in powder, the sulphate is taken in moistened rice wafers, or suspended in milk, or washed down with some tea, water, or preferably lemonade. It should not be wrapped in cigarette paper. In the form of powder it is inferior to solution by about 20 per cent., hence a larger dose has to be given to produce a corresponding effect. It is suited to those who have a great repugnance to the bitterness of the solution. The bitter taste and occasional irritant action of quinine on the stomach have led to the use of the drug in tabloids, tablets, capsules, pills, etc. It is a good rule to follow any one of these forms by a drink of lime juice or other acid beverage. Those who cannot swallow

sites when given in non-toxic doses—5 grains twice a day; 10 grains twice a day were effective but poisonous. The chief toxic symptoms are vomiting and diarrhœa.

There are two other products of cinchona bark made and used in India —*residual alkaloid* and *quinetum*. *Residual alkaloid*, as shown above (p. 256), is a mixture of the alkaloids precipitated after most of the quinine in *Cinchona ledgeriana* has been removed. *Quinetum*, like cinchona febrifuge, is a mixture of the alkaloids of cinchona, consisting principally of cinchonidine sulphate with smaller quantities of the sulphates of quinine and cinchonine, and containing likewise amorphous bases. Both the residual alkaloid and quinetum, when given in mixture, tend to cause nausea, due chiefly to the presence of quinoidine.

Tasteless preparations of quinine.—The tastelessness of these is due to their insolubility in water. They are useful for administration to children and others who cannot tolerate the bitterness of soluble salts. The chief drugs of this class are *euquinine* and *quinina*. The tannate of quinine is said to be practically useless in malaria, although it has been employed in Italy in combination with chocolate.

Euquinine (ethyl carbonate of quinine).—This is being used in India to a small extent instead of quinine. Its solubility is practically *nil*. As it is weaker than quinine it has to be given in doses one and a half times as large as the sulphate (8 grains = 5 grains quinine sulphate). It is less irritating to the stomach than the soluble salts. In the larger dose it is just as efficacious as quinine sulphate in malarial fevers and causes malaria parasites to disappear from the peripheral blood in the same way. Ten grains were given twice a day to five men suffering from malaria whose weight was just over 100 pounds; abundance of quinine appeared in the urine in each case, and after four days no trophozoites could be found in the blood.[1]

Much has been written about euquinine displacing quinine in the treatment of malaria. On a large scale in India this is only a remote possibility. It is much more expensive than quinine, and the quantity imported and the demands for it are very small.

Quinina, the alkaloid itself, is almost insoluble in water (1 in 1,560), therefore much less bitter than the soluble salts. It is absorbed as readily as the latter, and is about equal to quinine sulphate in efficacy in the treatment of malaria.

Many recent observations tend to indicate that the insoluble salts of quinine are therapeutically quite equal to the soluble salts in malaria. It is, however, generally considered that quinine in solution acts more quickly than the insoluble preparations. Solutions have to be employed when tablets, pills or powder cannot be swallowed.

Incompatibles.—Cinchona bark alkaloids and their salts are incompatible with alkalis, alkaline carbonates, and astringent infusions and decoctions.

Dosage.—When administered for the cure of malaria the dosage of the sulphate of quinine for children is:

Under 1 year	$\frac{3}{4}$—$1\frac{1}{2}$ grains
1—3 years	1—2 ,,
4—10 ,, ...	2—3 ,,
11—16 ,, ...	3—5 ,,

in each case four times a day.

The adult dose varies from 5 to 20 grains twice a day. In heavy infections

[1] W. FLETCHER, *Notes on the Treatment of Malaria with the Alkaloids of Cinchona* (1923), p. 23.

skin should be thoroughly washed with soap and water and then wiped with alcohol. When dry, tincture of iodine should be applied. It is preferable to use an all-glass syringe having a properly fitting glass piston and a gold or platinum needle. The syringes and needles may be kept *in a bottle containing absolute alcohol.* The alcohol is washed out with ether and then with sterile water. Or, just before use, the syringe and needle should be thoroughly boiled. Only the more soluble salts should be used. The solution to be injected should be sterilised by boiling, and when practicable made up fresh. In hospitals, where several such injections may have to be given to patients each day, it is necessary to keep a stock solution ready, preferably in small sealed glass tubes. For a stock solution the following is recommended: bihydrochloride of quinine, 100 grains; sterilised salt solution (0·75 per cent.), 300 minims. Thirty minims of this contains 10 grains. In hospitals single doses should be put up in ampoules and sterilised in an autoclave. If a glass tube be used the mouth should be covered with a sterilised rubber cap. Each tube should contain 2 c.c. of the solution (10 grains of the bihydrochloride). When using the tube the cap is disinfected, the needle is plunged through it, and 2 c.c. of the solution sucked into the barrel. "Sterilettes" and ampoules containing 15 grains of the bihydrochloride or hydrochloride in 2 c.c., others containing 7½ and 10 grains to the same quantity, are on the market. The end is broken off and the solution sucked into the syringe; they are convenient and reliable; the instructions accompanying them should be read carefully. A stoutish needle 2 inches or more in length with small calibre should be used; it should be inserted deep into the substance of the muscle. The writer strongly advises the adoption of the rule to use quinine ampoules or sterilettes from a good firm, and made-up solutions only when forced to do so.

Urethane-quinine in ampoules is recommended by some authorities as safe and non-irritating; others prefer the bihydrochloride of quinine and urea.

Many authorities consider that the solutions mentioned are too concentrated, lead to injury of muscle tissue, and sometimes to necrosis and abscess. Indeed, it is held that intramuscular injection always causes necrosis. While this is not a groundless objection, it is probably not so serious as has been represented. To obviate this there is suggested the use of a weaker solution, 10 to 15 grains of the bihydrochloride or hydrochloride of quinine being dissolved in 10 c.c. of 0·85 per cent. of salt solution. After intramuscular injection collodion should be applied and the area very gently massaged. It should take a few minutes to give the injection and complete the massage. The gluteus maximus is the muscle to select (avoiding the line of the great sciatic nerve), next the vastus externus about its middle on the outer side of the thigh, or the deltoid, avoiding the line of the musculo-spiral nerve. Usually the injections are not painful. Do not inject into the same place every day; this is a dangerous proceeding and certain to be followed by complications. When the neighbourhood of a previous injection site has to be used, inject in the circumference of a circle. The injection may be repeated every six hours or so until two, three or four doses have been administered.

When the paroxysms have ceased and parasites have disappeared from the peripheral blood the injections should be stopped. Children over two years of age tolerate intramuscular injections of quinine almost as well as adults.

There is much difference of opinion on this use of quinine. The writer has met with medical officers who use it in a high proportion of cases of malarial fever, even in the more innocent forms of malarial infection, and others who never use it at all. These extreme practices seem unreasonable. It is quite unjustifiable to use quinine intramuscularly in ordinary cases of malaria when

tablets, pills, etc., may crush them. Quinine is often wrongly accused of causing vomiting; this, however, is usually caused by the malaria itself.

The therapeutic effects of quinine are much the same whether the drug is administered in the liquid or the solid form provided that in either case it is swallowed, retained and absorbed. The writer has a slight preference in favour of the liquid form. If, in moderately severe cases of malaria, quinine in solution causes vomiting it should be given intramuscularly and repeated two or three times, and then tried in the tablet form by the mouth. The solid preparations given must be able to disintegrate speedily, otherwise they will be discharged from the alimentary tract unchanged; a rough test of this in the case of tablets, tabloids and pills is that they can be easily crushed, can be cut with a penknife, or readily disintegrate in water.

On the whole, too much stress has hitherto been laid on the therapeutic superiority of quinine in solution by the mouth as compared with tablets. The use of uncoated tablets has many advantages. The tablets of the Government factories and all British firms are so well prepared that they are absorbed almost as quickly as the solution. In 1923, on behalf of the British Red Cross Mission in Greece and Macedonia, the writer had much to do with the distribution and use of 3 tons of various soluble salts of quinine among malaria-infected Greek refugees. Much of this was in "tabloids" or in uncoated tablets made by four different British firms. The tabloids and tablets were from four to six years old; all acted satisfactorily, and produced the same effects on malaria parasites as the corresponding salts of fresh quinine in solution. It is rare to come across a brand of fraudulent quinine tablets from European firms. Those who condemn tablets can have had but little experience with them on a large scale. Sugar-coated tablets and tabloids are porous and a hygroscopic acid salt of quinine will burst them; hence under the sugar an impervious soluble coating of salol or stearin is usually applied, and as the absorption of quinine takes place almost exclusively in the intestine, there is little to object to in this. The writer prefers them uncoated. The use of tablets and tabloids is recommended in mild attacks of malaria, during convalescence, and for prophylaxis. It is preferable to have them fresh. If in doubt about their solubility they may be crushed to powder. Many practitioners have a prejudice against quinine pills unless they are freshly made up; the writer shares this antipathy. There is a great difference in solubility between ordinary uncoated quinine tablets and coated pills prepared in hospital pharmacies. The latter soon become hard and indigestible. Old coated pills are often found undigested in fæces, whereas uncoated tablets and tabloids are seldom discharged in this way. After the use of uncoated tablets or tabloids the Tanret-Mayer solution (p. 280) shows that quinine is contained in the urine in 2–2½ hours, is at its maximum in 5–10 hours, and has disappeared in 27 hours.

Quinine does not get a fair chance of absorption when the liver is sluggish. Hence the rule to give 2 or 3 grains of calomel (to adults), combined (when necessary) with a secretory cholagogue and a dose of Epsom salts, seidlitz powder, or some natural aperient water before commencing the quinine—except in very acute cases, or where perniciousness is present, when quinine must be given one way or another forthwith. The calomel induces a flow of bile, which is a solvent of the quinine.

After a full dose of quinine, in many cases the parasite will not be found in the blood the next day; in some cases it may not disappear for several days.

Intramuscular injection of quinine.—This form of administration of quinine must always be carried out with the strictest aseptic precautions. The

Intravenous injection of quinine.—The most rigid antiseptic precautions must be observed throughout, and everything must be sterilised at the time of making the injection. The bihydrochloride or the bihydrobromide of quinine is usually employed. The formula favoured by many is 10 to 15 grains of the bihydrochloride dissolved in 10 or 20 c.c. of sterile normal saline solution at blood temperature, this being repeated in three or four hours in very urgent cases, or six to eight hours in the less severe cases, if by that time oral administration is not feasible. Select a superficial vein at the bend of the elbow. "The secret of clean and easy puncture is a sharp needle and a prominent vein." Always examine the tip of the needle, even a new one, with a pocket lens. New needles are often quite useless. The solution should be sucked into the syringe and injected slowly. A fine needle should be used. On its introduction into the vein the plunger of the syringe should be slightly withdrawn to observe the entrance of blood into the barrel. It should take several minutes to complete the injection. If the dose is given too rapidly the pulse may become feeble and alarming symptoms set in. Some authorities advise the addition of adrenalin solution to counteract the fall of blood pressure that occurs. Many experienced practitioners prefer a much larger quantity of fluid, using either 100 or 200 c.c. containing 10 to 15 grains of the bihydrochloride. There are certainly some cases in which no amount of dilution of the solution, slow administration, or combination of cardiac or other stimulants seems to avert these alarming symptoms. In pernicious cases, where the blood pressure is already low, it may be well to begin with an intravenous dose of quinine and adrenalin at once and keep up the action by intramuscular injections, returning to oral administration as soon as this is feasible. In any case, if the pulse becomes bad during the injection, ether should be injected, and if the heart weakness is severe, strophanthin, digitalin or camphor should be given hypodermically.

In perniciousness of the choleraic, algid and adynamic forms the hydrochloride should be given in a much larger quantity of saline solution at blood temperature; 5 minims of a 1 in 1,000 solution of adrenalin may be added to the fluid.

Intravenous injection of quinine should be reserved for, but given unhesitatingly in, cases of special urgency—cerebral malaria with delirium or coma, or where this is threatening, malarial hyperpyrexia, overwhelming malarial toxæmia, and serious cases with persistent vomiting. Oral administration of quinine should be recommended as soon as the patient's state allows of it. Apart from the presence of perniciousness in malaria, intravenous administration of quinine should never be undertaken without grave reasons if the patient can take and absorb the drug given by the mouth.

In cerebral malaria and other forms of perniciousness, inhalation of amyl nitrite has been advocated to relax the arterioles and capillaries which are obstructed by parasites and allow the quinine in the circulation to get at the parasites in the red cells more freely. The writer doubts whether there is any therapeutic virtue in this procedure. A considerable proportion of cerebral malaria cases have no blocking of the capillaries, we are unable to diagnose in which cases obstruction exists, and 90 per cent. of the quinine given intravenously ceases to be recognisable in the circulation as quinine within a minute or so after its introduction. Besides, it is doubtful whether anyone knows what the action of amyl nitrite is on cerebral capillaries. After intravenous injection there is usually considerable destruction of parasites with liberation of toxins, and this may give rise to further distressing symptoms, especially cyanosis and dyspnœa. Fortunately this seldom occurs. If such symptoms arise it may be inferred that the action of the heart is seriously interfered with, and the heart muscle may cease to act. The writer agrees with

the patient can take the drug by the mouth. It is equally unjustifiable to withhold these injections when they are indicated. The intramuscular injection of quinine should be reserved for severe cases of malignant tertian malaria, pernicious attacks where the drug cannot be given orally on account of non-absorption from vomiting or gastritis, the presence of severe malarial toxæmia, exceptionally large number of parasites in the peripheral blood unaffected or only slightly affected by oral quinine, really intractable cases of the more innocent forms of malaria, and persistent relapses. In the last two it often acts like a charm.

Intramuscular injection is sometimes very painful and is occasionally followed by necrosis of muscle tissue. The writer has seen four men in a malaria hospital of 150 beds with large, hard lumps on the buttocks and other sites of injection. There was no question of local infection in these cases, as the injections were given under rigid antiseptic precautions by highly trained medical officers. Hundreds of these injections had been given. On the other hand, a medical practitioner in Central America gave many thousands of intramuscular injections of quinine with nothing more serious than a very occasional necrosis followed by abscess.[1] The author's experience is that these lumps occur in less than 1 per cent. of the cases, and, considering the large number of lives saved and suffering relieved by this method of administering quinine, it would be regrettable if prejudice against it became generalised. There is, however, one serious point to deliberate on. We cannot tell beforehand whether in any particular case necrosis of muscular tissue will occur from injection of quinine, although it happens more frequently in the anæmic, debilitated and badly nourished. If, in grave malaria, the case is one in which the quinine (or acid in it) necrotises the muscle tissue and is contained in the destroyed part, and therefore of no use to the patient, he may lose his life. This indicates that where an immediate and reliable effect is called for, intravenous injection should have preference over intramuscular. It is unfortunately the case that at present we do not know what conditions determine that in some cases serious damage or necrosis of muscle tissue will occur after intramuscular injections, while in others it will not. The writer has never seen tetanus follow intramuscular injection, but several cases of this catastrophe are on record. Intramuscular injection should never be given without serious consideration, as there is always a certain amount of risk. The method is valuable in malaria, but it must not be used indiscriminately.

Sir Leonard Rogers recommends cinchonine bihydrochloride for intramuscular injection. He considers that it is more rapidly absorbed, is less injurious to muscle tissue, is less painful than other salts, is not followed by induration, and is almost as plasmodicidal as the corresponding quinine salt. He advises 10 to 15 grains in 1½ to 2 c.c., injecting this into the deltoid once a day for four consecutive days, after which the acute symptoms yield and oral quinine is commenced. Intramuscular injections of quinine seldom cause severe cinchonism, on account of the slow absorption of the quinine. They should never be given by nurses, ward orderlies or sick attendants.

In view of the very great difference of opinion as to the local effects of quinine injected into muscle tissue this question must be placed on a much more definite basis than it is before there can be conviction as to the value of this method of administering quinine, inquiry being specially directed to the conditions in which quinine is likely to cause necrosis and be useless to the patient, either for absorption or metabolism, and to those in which it can with confidence and safety be used therapeutically.

[1] *International Conference on Health Problems in Tropical America*, 1924; Dr. N. P. Macphail, *Intramuscular Injections of Quinine*, p. 106

per rectum. It should not be given by this route if any other means are available." He found that in some cases it gave rise in Malayans to acute inflammation or sloughing of the rectal mucous membrane.

Toxic effects of quinine.—Cinchonism (quinism) is the term applied to a group of toxic symptoms following the prolonged administration of quinine, or after a very large dose, or even after a small dose in those who have a special idiosyncrasy to the drug. It resembles salicylism. The patient is more or less deaf but complains of ringing in the ears and headache, which may be very severe, vision and equilibrium are disturbed, and there may be gastro-intestinal irritation. In poisonous doses there may be bleeding from the nose, erythema, delirium, coma, and even death from cardiac failure. In cases with an idiosyncrasy it is well to add some dilute hydrobromic acid to the quinine mixture.

Actual dangerous symptoms of quinine poisoning are rarely met with. The writer has on only four occasions met with alarming symptoms from large doses. All four had taken from 35 to 52 grains in twenty-four hours. The general effects were—trembling, pallor, agitation, restlessness, anxiety, profuse sweating, palpitation, weak and frequent pulse; in one there was temporary collapse. In very large doses quinine is a cardiac depressant and causes a fall of blood pressure. This is specially to be remembered when giving the drug intravenously to those who are greatly debilitated or advanced in years. The author is convinced that on the plains of India during the hot weather it would be dangerous to give the enormous daily doses (90 to 100 grains) that were given in England during the Great War in some of the groups of cases in which endeavours were made to ascertain the best method of using quinine for the prevention of relapses. The best general preventive of quinism is caffeine, given internally or hypodermically half an hour before giving the quinine; the next best is bromide of potassium.

Quinine fever—so-called.—Much has been written about *quinine fever* in the last quarter of a century. By this term is meant pyrexial phenomena without any or only few malaria parasites in the peripheral blood of patients taking small or medium-sized doses of quinine. The writer doubts if quinine has anything to do with the fever in these cases; in most of them an increase in the quantity of the drug given daily for three or four days would remove it.

It will sometimes be found that a patient with an old infection taking quinine during the intervals of relapses complains that the drug is upsetting his digestion and disagreeing with him generally. In a number of these cases the patient is working up for another bout of paroxysms, and an increase of the doses of quinine, or a change of the quinine salt from, say, the sulphate to the hydrochloride, removes his discomforts. Rarely do we come across a case with genuine idiosyncrasy for quinine. It takes one of several forms—a cutaneous eruption (urticarial or erythematous), the usual form, irritation of the stomach with vomiting, or cinchonism. The solution may cause vomiting when tablets do not. The writer has never met a genuine case of quinine idiosyncrasy associated with fainting, collapse, cold sweats and great fall of blood pressure after a comparatively small dose, but he knows that they do exist; four experienced medical officers in India told him of cases they had treated, and referred to them as being very alarming and calling immediately for cardiac stimulants and treatment for collapse.

Quinine during pregnancy.—Pregnant women can take quinine, and provided parasites are found and infection is moderate with mild symptoms, it should be administered to them with care, and in smaller doses than in ordinary cases. When the symptoms are severe, full doses may become necessary. Large doses should never be given to commence with in moderate infections with ordinary symptoms. Large doses occasionally cause miscarriage,

MANSON-BAHR[1] completely, that in heart cases a preliminary intramuscular injection of quinine should be given, to be followed in six or eight hours by a small intravenous injection (5 grains); there are some cases in which this is the only way of saving life. If full intravenous doses are given in these heart cases there is much risk of cardiac failure following. The large majority of practitioners agree that intravenous injections of quinine should be adopted when prompt action is necessary to save life; for it is generally considered to be the speediest and most certain way of introducing quinine into the system, of attacking the parasites, and of controlling the symptoms in serious cases of malaria. *Prima facie* the results should be more certain and obtained in less time than by other methods of administration, and in the writer's experience this is certainly the case. We shall see, however, that these claims for it are debateable.

Assuming that quinine acts directly on malaria parasites, we emphatically want the biochemist to discover for us some means of injecting the drug so that it can be tolerated by the tissues, diffuse quickly throughout the body, and be readily assimilated. It appears to the writer that something is required to facilitate the solution of the quinine base in normal saline; he knows that some of our leading quinologists and pharmaceutical chemists are working on this subject at the present time. It is of vast importance; once solved, we will be shorn of all our anxieties regarding intramuscular injection of quinine and some of those connected with intravenous injections. But is the assumption that quinine acts directly on parasites well founded? (See pp. 268–270.)

Hypodermic injection of quinine.—Quinine should never be used hypodermically in India. Regarding this method there is no compromise; it is absolutely condemned. Subcutaneous injection of quinine has been followed by extensive and dangerous abscess or suppuration, necrosis or tetanus.

Quinine per rectum.—This is the least satisfactory way of administering quinine. It may be employed when there is severe and persistent vomiting and other methods are contra-indicated. About three times the normal dose is required. Be sure there is no diarrhœa or bowel irritation. In the adult about 30 grains of quinine in warm solution (strength 1 grain to 1 drachm) with 10 minims of laudanum is the ordinary dose, repeated in four hours; it should be injected slowly through a rubber tube or catheter. Rectal injections may be used in milder infections where vomiting is present, but only so long as the vomiting lasts; when it ceases quinine should be given in tabloids or tablets. Sometimes this method is useful in children; a child of two years would require 5 grains in warm solution repeated every two hours for four doses; a drop of tinct. opii may be added and the injection given through the nozzle of a glycerine syringe. It is only to be used to tide over a temporary difficulty. As tested by the amount excreted in the urine, only a small percentage of the quinine is utilised in the body by this method, although some authorities state that cinchonism may be rapid after it. Occasionally quinine given per rectum causes damage to the mucous membrane. W. FLETCHER,[2] after a special investigation of this method, states: "Absorption of quinine by the rectum as judged by the effects of Mayer's reagent on the urine is poor, irregular and unreliable, and as judged by the effect on parasites in the blood not to be relied on. In eleven of sixteen patients on whom it was tried for a week parasites were still present; under quinine by the mouth they disappeared at once. Quinine is too irritating for administration

[1] MANSON'S *Tropical Diseases*, 8th Ed., pp. 82, 83.

[2] "Rectal Injection of Quinine," *Bull Inst. Med. Res., Federated Malay States*, 1924, i, p. 20. This is an important record, which should be consulted. See also *Trop. Dis. Bull.*, October, 1925, p. 815.

most of it is eliminated in eight to ten hours. An important point is that the elimination is most rapid during the first six hours.

It is widely held that a soluble salt is more efficacious in malaria than an insoluble one. There is now in existence evidence that at least throws some doubt on this statement; the general evidence is that excretion, and so presumably absorption, of quinine is as rapid after oral ingestion of an insoluble as of a soluble salt.

The action of quinine on the blood itself, apart from its action on malaria parasites, is complex and important. It markedly influences the stability of the compounds of the hæmoglobin with oxygen. It interferes with oxidation, hence oxyhæmoglobin is relatively unable to give up its oxygen to the tissues, the metabolism of which is thereby modified. This may explain part of its antipyretic action. It reduces the amœboid activity of the white blood cells (but see p. 270), hence it checks diapedesis of leucocytes. The diminution of leucocytic movement is regarded as a sign of reduced metabolism within the cells. In very large doses it weakens the intracardiac ganglia, slows and weakens the pulse, and dangerously lowers the blood pressure. It is antipyretic, but not antithermal. This action is not due to its effects on the thermal centres, nor to diaphoresis, but to the influence of the quinine on the stability of the oxyhæmoglobin. The antipyretic effect is produced in about two hours. The influence of quinine on malarial temperature is due to an entirely different cause.

Various opinions as to how quinine destroys malaria parasites.—J. Morgenroth considers that quinine has a specific chemotherapeutic action in malaria. He doubts whether it is the small amount of quinine in the plasma that destroys the parasites; nor does he share the view that it is the quinine in the viscera that does this. From a series of experiments he concludes that quinine is stored or held in the red blood cells, and that both the therapeutic and prophylactic effects of the drug are due to the negative chemotaxy or repulsion exercised by the cinchonised red blood cells on the attacking parasites. C. C. Bass is of opinion that quinine makes the red cells permeable to the lytic action of the serum. Some of the recently published evidence seems to indicate that quinine acts indirectly in some way, possibly as a metabolite; pharmacological chemists and biochemists assure us that it is quite possible to put this to the test.

Does quinine act directly on parasites in the blood?—The basis on which many forms of quinine treatment are carried out is the assumption that quinine acts chiefly on extra-corpuscular parasites. Certain forms of treatment aim at so giving the quinine that it shall be present in the blood in maximum concentration at the time of sporulation. But this view includes the problematical assumption that quinine is plasmodicidal in the strengths detected in the blood. The literature on the subject does not give much evidence that these extra-corpuscular forms are more vulnerable to quinine than are the intra-corpuscular ones. Nor has any serious effort been made to find out whether such systems of treatment do, in fact, produce maximum concentration of quinine in the plasma at the desired moment.

Lt.-Col. Clayton Lane, I.M.S.,[1] has lucidly pointed out that our knowledge regarding the varying degree of concentration in the blood under different methods of administration is still very meagre, and we have very little exact information as to the time relation of this to dosage. Nor have we much beyond practical and clinical experience as evidence to indicate at what stage of the parasite's life-cycle in the blood it is most vulnerable. He suggests that, with cultures containing increasing percentages of quinine, it should be possible to observe whether development was checked at the extra-corpuscular stage, and

[1] *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. 18, No. 7, January, 1925, p. 300.

but if the malaria goes on untreated by quinine, there is more risk of abortion. It is, as a rule, quite safe to begin with a minimum quantity of 3 grains, increasing it, if necessary, to 5 grains or more three times a day; 5 to 10 *minims of laudanum or 10 grains of bromide of sodium may be added if* indicated. The sooner the necessary quantity is got into the system with safety the better. Pregnant women should remain in bed while taking quinine. *In some cases the first paroxysm of malarial fever comes on during parturition*, and in malarious places relapses are not uncommon at that time. Malaria causes hundreds of thousands of abortions in India yearly (see pp. 36 and 200) in the absence of quinine treatment.

There is a difference of opinion among the best authorities as to whether more quinine is present in the plasma or in the red blood cells during the time the drug is circulating. It would appear that the plasma and red blood cells contain about the same amount of quinine. The rapid absorption and rapid elimination of quinine is considered by most authorities to be of great practical importance, as on these should depend the *time at which the drug should be given in each case of malaria*, so as to get the maximum effect on the parasite at that stage in which it is most vulnerable. Except in large hospitals, quinine can rarely be given in relation to the life-history of the parasite in the patient's blood. Nor can it be stated that this practice of giving quinine in relation to the life-cycle of the parasite is actually based on scientific observations. Little as we know regarding oral administration, we have even less information as to what happens to quinine in the body when it is given intravenously and intramuscularly. It is presumed that the useful part of the dose is that which goes through the circulation; we require to introduce a sufficient amount into the blood in the shortest time possible to bring about the destruction of the parasite. Here, however, we have another complication. Quinine given intravenously leaves the circulation more rapidly than when otherwise administered. RAMSDEN and LIPKIN [1] state that 90 per cent. of the quinine given in this way disappears from the blood within a minute. Accordingly, to be completely effective it would seem that there should be most accurate timing of the administration, which would require knowledge of the life-history of the parasite in the receiver of the quinine. This is the reason for supplementing intravenous quinine by orally given doses, which should follow close on the injected dose if the patient can swallow.

Digestion, absorption, metabolism and elimination of quinine.—Quinine orally administered is mainly absorbed in the small intestine; this absorption is rapid and complete, even in the case of those salts of quinine that are not soluble in water. "Very little quinine is absorbed in the stomach; no matter what salt is swallowed it passes on into the duodenum, where it is precipitated as amorphous quinine base and is absorbed by the aid of the bile." [2] Most of the quinine administered is absorbed within six hours after being taken; absorption is less rapid if taken on a full stomach, or as one of the more insoluble salts such as euquinine, which require to be hydrolysed by the alkali of the duodenum. It passes into the blood from the alimentary canal unchanged, but its stay there is short; a large share of it, probably as much as 60 per cent., is rapidly taken up by certain internal organs, especially the liver, spleen, suprarenal bodies, kidneys and brain, in which the quinine molecule is split up and the drug destroyed. The undestroyed part passes through the circulatory system and is eliminated unchanged in the urine, in which secretion it may be found within half an hour of being taken, and

[1] *Annals of Trop. Med and Paras.*, Vol. IX, 1918, pp. 434–64.
[2] Prof. W. E. DIXON, Address, British Medical Association Meeting, 1920.

and secondly, a capacity on the part of the host to respond to the antigen by the formation of a sufficient quantity of immune-body. If for any reason either of these two requirements is not satisfied, the infection is not completely eradicated and a relapse occurs. The effect of quinine is more marked when parasites are numerous in, than when they are absent from, the blood. The second requirement for the production of cure is that the cells or tissues of the host shall be able, in response to the antigen stimulus, to produce a sufficient quantity of immune-body. That the human host exhibits a certain degree of natural immunity to malarial infection, and that this is capable of being increased in response to the proper stimulus, there can be little doubt.

C. F. Craig,[1] after a careful study of the action of quinine on malaria parasites in fresh and stained specimens, records the opinion that it affects the parasite injuriously during all stages in man except just prior to sporulation. The sporulating body is not affected and sporulation occurs, but most of the spores are destroyed by the drug in the blood plasma. He advises giving quinine in divided doses at regular intervals of time rather than in one or more large doses at long periods. The writer much doubts the value of this method of administration and disagrees with the assumption on which it is based.

Another theory regarding the action of quinine in malaria was recently communicated to the writer by a malaria authority. "Quinine acts on all red cells, those containing parasites and those not, altering, say, the lipoidal surface layer; they thus become foreign bodies, and so are filtered out by the spleen and lungs; hence the disappearance of parasites. It is at least hypothetical to say they are destroyed; all we know is that they disappear. This entails a rapid reproduction of red cells by marrow, etc."

The author's views regarding the action of quinine on malaria parasites.[2]—The object of giving quinine is to kill the parasites. So far as we know at present, except when given intravenously (see pp. 264, 265), the greatest part of the dose of quinine does not reach the blood for a few hours after its administration; and as its slow excretion from the blood begins at the same time that it reaches that fluid, the fullest possible doses should be given when decided effects are required (as in pernicious attacks). These remarks emphasise the uselessness of small doses when a pronounced effect is demanded, unless these are repeated sufficiently often.

Quinine is the universally accepted curative drug for malarial fevers; and it is for this purpose the nearest approach to a specific that we possess. It is believed by most authorities that it has a decided and distinct influence on malaria by killing the plasmodia of the disease in the blood. There is great divergence of opinion as to the way in which quinine affects the malaria parasite. The following paragraphs attempt to give an epitome of the more important views held on the subject.

Quinine destroys the parasites in the body either directly or indirectly. The other effects of the drug on the human economy in malarial fevers are quite insignificant compared with this main action. Some authorities state that it paralyses the white blood cells. The writer is unable to accept this; he agrees with those who consider that quinine accelerates the phagocytosis of malaria parasites. Large mononuclear cells are found at certain stages of malarial fever containing melanin, and they may be seen on fresh slide preparations in the act of engulfing melanin in cases that are taking full doses of quinine.

In the blood "the spores are the most sensitive (to the action of quinine); then come the large organisms that have completely replaced the blood corpuscles, and finally the endoglobular young forms, for which the blood corpuscle

[1] *Malarial Fevers*, p. 369. [2] *Prophylaxis of Malaria in India*, p. 156 *et seq.*

if it were so, whether the concentration concerned had any relationship to that which is found in circulating blood after the administration of quinine. If it were not quinine itself, but, as the facts suggest, some metabolite of it which was plasmodicidal, then the more excreted in the urine, the less metabolite was presumably formed. On the same supposition, since metabolism of quinine is effected principally in the intestines, liver and kidneys, the drug's efficacy would depend, not on its solubility, but on the facility for metabolism of the form used. "It is not known whether the quinine which is stored up and metabolised in the organs takes part in the destruction of parasites or not; most observers consider that it does not, and that the only useful portion of the drug is that which escapes destruction in the organs and passes through the circulatory system." [1]

Quinine *in vitro* in stronger solution than can ever be met with in the blood stream does not destroy all malaria parasites. A mixture of equal parts of defibrinated simple tertian blood and a 1 in 5,000 solution of quinine was still infective after incubation for twelve hours at 37° C., and if the strength of the solution was doubled, infection was still possible after five hours (MUHLENS and KIRSCHBAUM, 1924). WARRINGTON YORKE and MACFIE have confirmed these observations. Quinine given to a donor of malarial blood before taking his blood does not render the blood harmless to the receiver. The inference deduced by some authorities is that, after absorption, quinine is in some way changed by the body cells into a substance that is lethal to malaria parasites; they consider that the observations quoted are opposed to a direct plasmodicidal action of quinine and in favour of MORGENROTH's pharmacodynamic action of the drug. RAMSDEN (1918) also found that it is extremely difficult to get a higher concentration in the blood than 10 mgm. per litre, that is 1 in 500,000 of blood and 1 in 250,000 of the plasma. A concentration of 11 mgm. caused severe toxic symptoms. He states that failure to sterilise the blood is not due to failure to attain (within the limits of the tolerable) sufficient concentration of quinine in the blood, and no concentration can be relied upon to effect a permanent cure.

"In all probability quinine has little effect on parasites in red cells in the capillaries of internal organs and deeper tissues; RAMSDEN and LIPKIN have adduced evidence bearing on the possibility that in the blood-vascular system there are regions which are kept almost free from quinine throughout a period of the quinine treatment." [2] This would at least partly explain the difficulty of completely eradicating malaria in some cases. It is now practically certain that the peripheral blood does not represent the visceral blood; *e.g.* if a rabbit is given CO to breathe, none is found in the spleen when it is killed, but if the rabbit kicked its hind legs vigorously and spontaneously when held by the ears, then CO is found in the spleen.

WARRINGTON YORKE and MACFIE, as has been indicated (pp. 44, 45), believe that the following train of events occurs: Quinine given to a person with parasites always destroys directly, or more probably indirectly, large numbers but not all, thus setting free a considerable quantity of soluble antigen. The antigen provokes, by stimulation of the host's tissues, the formation of immune-body. The immune-body, if present in sufficient amount, destroys the remaining parasites, thus resulting in sterilisation of the infection and the cure of the patient. For the cure to occur this view requires, first, the setting free of a quantity of soluble antigen by the destruction of a large number of parasites,

[1] Lt.-Col. CLAYTON LANE, I.M.S., *Trans. Roy. Soc. Trop. Med and Hyg.*, Vol. 18, No. 7, January, 1925, p. 353.

[2] Lt.-Col. S. P. JAMES, I.M.S., in BYAM and ARCHIBALD's *Practice of Medicine in the Tropics*, Vol. II, p. 1034.

has no direct destructive action upon the crescents, but it reduces their number to less than 1 per cent. if given daily in doses of 20–30 grains for three weeks; this action is believed to be due to the cutting off of the source of supply by killing the asexual forms.

W. M. JAMES[1] considers *that the development of gametocytes* in all three species is not morphologically affected by quinine; that what happens is that *the source of supply is cut off*, but those gametes that have already begun to develop from the asexual forms will continue in their growth irrespective of treatment. A red cell is estimated to have a life of thirty days, though estimates vary considerably; hence, presumably a crescent cannot live longer unless the dead red cell adheres to the crescent.

MÜHLENS and KIRSCHBAUM have shown tolerance of crescents to quinine in that in winter and in Europe they transmitted sub-tertian malaria through *A. maculipennis* to a fresh case, the donor, at the time when he infected the mosquito, being under the influence of quinine.[2]

The work summarised by MAYNE[3] strongly suggests that the giving of quinine to gametocyte-carriers prevents subsequent development in Anopheles of *P. vivax*, but not of *P. falciparum*, and it carries the corollary that, given to an individual with mixed tertian infection, quinine will probably destroy his malignant tertian parasites, but that so long as the crescents exist he will be capable of spreading the infection and be a danger to others. At the same time, although it will probably not cure his benign infection, it will, so long as he takes it, emasculate his benign gametes so that there is no risk of his passing this infection on to others. WENYON has independently published identical conclusions.

STANDARD QUININE TREATMENTS

General remarks.—A standard quinine treatment for malaria that brings about disinfestation with the minimum quantity of the drug in a reasonably short time is urgently called for on the grounds of economy and efficiency. No such treatment has yet been discovered. In the *Memorandum on the Treatment of Malaria* issued by the War Office in 1917 it was stated that no line of treatment which had been tried in the Army up to that time had sufficed to eradicate the infection entirely in more than a small percentage of cases, and no clear indication had been obtained that any one line of treatment was much better in this respect than another. This dictum holds good to-day. With a disease subject to so many variations it seems rather unreasonable to expect all cases to respond in the same way to a standard plan of quinine treatment. A certain very small percentage of cases of malaria will be *cured* of their infection after quinine treatment for ten days only, a higher percentage after four weeks' treatment, a considerably higher one after eight weeks' treatment, and the percentage of uncured cases after twelve weeks' treatment will be small.

With a view to discovering the best method of quinine treatment, varying quantities of quinine have been administered in different ways over certain periods and the percentage of recoveries compared. It will be obvious that, as we cannot state that disinfection has been achieved, therefore the apparent "cure" may not be complete. *Cure* usually signifies freedom from relapse paroxysms and from parasites after treatment has ceased over a test period, usually two months. But many points are overlooked in arriving at conclusions in these groups of cases. One point is *season of the year*. It has been found that, of cases of malaria invalided during the War to England and treated with full doses of quinine from July to September, only 38 per cent.

[1] *International Conference on Health Problems in Tropical America*, 1924, p. 87.
[2] *Trop. Dis. Bull.*, 1923, Vol. 20, p. 777. [3] *Ibid.*, 1919, Vol. 16, p. 310.

acts as a protecting mantle. GOLGI found the endoglobular young forms of the tertian parasite very sensitive, and he concludes that the hypertrophy of the blood corpuscle produces a relaxation of the structure which permits the quinine to pass through it."[1] Quinine causes a degeneration of the parasite which is especially marked in the younger forms, and is most marked at the time of segmentation. It acts upon the malaria parasite in that phase of the life-cycle in which it is being nourished and developed. "When the nutritive activities cease by an arrest of the transformation of hæmoglobin into melanin, and the reproductive phase begins, quinine is inefficient in its action."[2] Quinine is specially active from the time of segmentation until pigmentation commences within the red cell. Under the action of quinine there is a loss of amœboid activity in the parasites in the blood, and a granular degeneration of the intra-corpuscular forms; the intensity of the staining is lessened, and this is specially the case with regard to the chromatin, which does not occur in blocks or clumps, but as small dots or granules irregularly scattered; the blue margins of the parasites are more defined, and are seen as little lumps or knots at the circumference, while the pigment occurs as fine dots. A special effect of quinine observable in stained preparations of the ring forms of all malaria parasites is that the white vesicular part of the nucleolus stains blue. Such changes are best seen in simple tertian and quartan under quinine, but they are also seen in malignant tertian. "In malignant tertian the young amœboid forms appear greatly shrunken, their protoplasm more or less granular, and amœboid motion is lost."

The amœbulæ thrown into the blood plasma during sporulation are highly susceptible to the lethal effects of quinine, the intra-corpuscular forms less so. A single large dose of quinine, given just before a paroxysm of either simple tertian or quartan is expected, will destroy most of the young brood, without modifying the current attack of fever. It has little or no effect on the fully developed schizont and it does not prevent its sporulating.

To get the full effects of the quinine on the parasite it should be in the blood at the time of sporulation to destroy the spores, sporonts, and possibly some of the younger schizonts. An unknown number of schizonts certainly escape the action of the quinine. Whatever quinine does, we know that if it is absorbed it causes all parasites except the sexual forms of malignant tertian malaria to disappear from the peripheral circulation in a few days, in a high percentage of malarial fever cases, if re-infection is prevented.

Quinine is less lethal to the older forms of the schizont, and twenty-four hours or more may elapse before the full effects of quinine given orally are manifest. Sometimes the anxious medical attendant mistrusts this use of the drug and impatiently flies to intravenous or intramuscular injection to supplement that given by the mouth.

Quinine, if absorbed, acts within a few days. Its absorption can be checked by testing the urine. If absorbed and yet not removing fever, the case, in the absence of parasites in the circulation, should in practice be considered as non-malarial. Nevertheless cases are occasionally met with in which it is extremely difficult to decide whether they are malarial or not. We should not, therefore, consider the rule stated as rigid and absolute. Over-dosage does harm both in malarial and non-malarial illnesses.

Action of quinine on gametes.—According to D. THOMSON, quinine

[1] MANNABERG, *The Malarial Parasites*, New Sydenham Soc. Translation, by Dr. R. W. Felkin, p. 193.

[2] MARCHIAFAVA and BIGNAMI, article *Malaria* in *Twentieth-Century Practice of Medicine*, Vol. XIX, p. 402.

Third and *fourth weeks*.—10 grains daily with 20 grains every seventh day instead of 10.

Fifth to *eighth weeks* (inclusive).—10 grains daily.

Ninth and *tenth weeks*.—5 grains daily with 10 grains on two consecutive days each week instead of 5.

Eleventh and *twelfth weeks*.—5 grains daily with 10 grains instead of 5 once a week.

Should a relapse or a re-infection occur while the patient is under this treatment, the whole course is to be commenced *de novo*.

These rules are general and not specific. The quantities mentioned are what the writer considers the average patient should take. Some will require more, others less. There are many factors entering into the circumstances of cases of malaria that will necessitate some modification of this method. Amongst these are the freshness of the infection at one end and chronicity at the other, inordinate sensitiveness to the toxins metabolised by malaria parasites, unusual susceptibility to the effects of quinine, quitting the malarious for a non-malarious locality, etc. It is not possible to formulate any rules for quinine administration for three months that would cover the peculiarities met with in all patients.

The writer is disposed to think that, provided the quinine is continued daily for the period named, a smaller dosage of the drug may suffice during the latter half of the course; he is, however, not prepared to recommend this change until it is properly tested; he has never tried it. It will be found that there is an undetermined, but probably small, percentage of cases that will require a four months' course; the anamnesis of each case of relapse will show which cases these are.

Many authorities consider that it matters very little whether the weekly quantity advised above is concentrated into two days or three days a week; there will be little difference in the results, but the full weekly dosage must be rigidly observed. The writer has a decided preference for the daily dose; the great advantage of the smaller doses is that they can usually be taken without any serious digestive disturbance, headache, ringing in the ears, and so forth.

U.S. National Malaria Commission's standard course.—This is the course recommended by C. C. Bass (1921). Thirty grains of quinine sulphate daily so long as clinical symptoms of malarial fever continue, or for three or four days, in three doses of 10 grains each, and thereafter 10 grains nightly, before retiring, for eight weeks. For infected persons not having acute symptoms only the eight weeks' treatment is required. The sulphate is given in the form of capsules of 3, 4 or 5 grains, one or two capsules being taken according to age; 112 capsules are issued as a full course. This is an arbitrary mean between complete sterilisation and an entirely inadequate course which will leave a high percentage of cases liable to relapses. This course disinfects 90 per cent. of cases; over three months' treatment is required to cure the remaining 10 per cent. The same results would be obtained in ordinary cases of malaria in India, without re-infection, but probably the percentage of relapses would be higher. It would fail in the *epidemic* and *hyperendemic malaria* of India.

Panama Canal Zone standard course of 1925.—Put the patient to bed, give 2–3 grains of calomel, followed by a dose of Epsom salts. As soon as diagnosis is settled, 15 grains of quinine are given *t.d.s.*; the quinine is continued for a week, or until the temperature has been normal for five or six days. Then 10 grains are given *t.d.s.* for ten to twelve days. It is recognised that the treatment of concomitant infections, such as syphilis and ankylosotomiasis, is essential, especially in chronic malaria. It is considered that by employing

relapsed; under the same treatment, from January to April 93 per cent. relapsed. Failure to make allowance for this fundamental seasonal effect vitiates the results arrived at in a great deal of the experimental work on the subject. These treatments in Liverpool, and probably a similar series in Macedonia, were not primary cases, but relapses. In treating primary cases in England, deliberately induced in general paralytics, such a seasonal evidence of curability did not show itself in WARRINGTON YORKE's experience, but this is no evidence against the relation of season to cure of old infections, because induced primary infections are ALL cured with a comparatively small amount of quinine, except those infected through Anopheles.

In an endemic malarious locality, when the parasites of malaria have once increased to sufficient numbers to produce malarial fever, they are difficult to get rid of permanently. The writer believes malaria, especially benign tertian malaria, to be one of the most difficult of infective diseases to eradicate in these conditions. Nothing short of a three months' course during the non-malarial season, and a *four* months' course during the malarial season (when it is assumed re-infections are repeatedly occurring), is sufficient for this purpose. This duration of treatment is important, anyhow in India.

The rationale of quinine after-treatment is based on the assumption that all the parasites are not killed during the active stage of the treatment. Some parasites continue to multiply, but under quinine in fewer numbers, becoming so few as not to be found in the peripheral blood, and finally disappearing.

It is proposed to describe some of the standard quinine treatments suggested at different times and in various countries, beginning with that which the writer has found the most effective.

Author's standard course of quinine in malaria in India.—The following is the general plan of a three months' course of curative quinine treatment. The writer advocated it in 1909, and he still considers it the best that can be used in India for eradicating malarial infection.

First week.—

(*a*) In *double malignant tertian* (quotidian), 30 grains[1] daily for three days, and then 20 grains daily for another three days, none on the seventh day, making 150 grains during the first week.

(*b*) For *ordinary malignant tertian*, 30 grains[1] on the day of the next expected attack, and continued on alternate days until 120 grains have been taken during the first week.

(*c*) For *double benign tertian*, 30 grains daily for three days, and then 20 grains daily for three days, none on the seventh day, making 150 grains in the first week.

(*d*) For *ordinary benign tertian*, 30 grains[1] on the day of the next expected attack and continued on alternate days until 120 grains have been taken during the first week.

(*e*) For *ordinary quartan*, 30 grains[1] on the day of the next expected attack and continued every third day until 90 grains have been taken. For double and triple quartan the intervals between the doses would be shorter, and the amount of quinine to be administered in the first stage of the course larger.

From the end of the first week the course may be the same for all types of malarial infection.

Second week.—15 grains daily.

[1] For ordinary cases the 30 grains taken in two 15-grain doses give as good results as in three 10-grain doses. Given in tabloids, tablets or powder in moistened rice wafers the results are almost, if not quite, as good as in solution.

mosquito bites has shown that in primary attacks the amount of quinine which will frequently effect complete disinfestation does not exceed a total of 90 grains. In cases induced by injection of infected blood its completely curative effect is much more marked.

QUININE IN THE PREVENTION OF RELAPSES

General remarks.—The objects aimed at in quinine treatment and after-treatment of malarial fevers are to relieve the symptoms of the paroxysms, and to disinfect the patient, thus preventing relapses and the transmission of the disease to others through anopheline vectors.

If all primary infections were really cured (see p. 245), the incidence of malaria would diminish, and it would probably eventually be eradicated. This is the ideal to be arrived at, although it is not likely to be achieved. The difficulty in preventing relapses must be carefully distinguished from that of bringing about the cessation of paroxysms. As will be seen from the Tables given on pp. 13 and 14, only 23·5 per cent. of the cases coming under treatment in endemic malarious areas are primary infections; 76·5 per cent. are relapses and re-infections.

The story is quite different when the absence of re-infections can be assured. Of this we have wide experience in British troops laden with malaria who are sent to non-malarial hill stations, where, after a long course of quinine and a three or four months' residence, they return to the plains in the late autumn, and in the great majority of cases remain free from malaria until re-infected during the following year. It was also typically seen during the Great War in the British battalions sent from Salonica to England saturated with malaria; they were given 15 grains of quinine daily for two weeks, followed by 60 grains a week for two months; this course enabled nearly all to return to the fighting line.

The Liverpool cases treated during the Great War were given quinine in doses varying from five to 120 daily. The results and methods of administration are shown in the following Table [1]:

Table Summarising the Result of Various Short Courses of Quinine in the Treatment of Simple Tertian Malaria obtained at Liverpool during the War · Post-Treatment Observation Period at least Two Months.

From WARRINGTON YORKE and J. W. S. MACFIE

Daily dose in grains and salt of quinine used.	Method of administration.	Number of consecutive days quinine given	Number of cases treated.	Number of relapses.	Percentage of relapses.
5 sulphate . .	Oral	2	12	11	91·6
5 hydrochloride .	Oral	2	18	18	100
10 sulphate . .	Oral	2	10	10	100
15 sulphate .	Oral	2	14	14	100
15 hydrochloride	Intramuscular	2	20	19	95
15 alkaloid	Intramuscular	1–2	38	31	81·6
30 sulphate .	Oral	2	14	14	100
45 sulphate	Oral	2	12	9–12	75–100
60 sulphate . .	Oral	2	12	7	58
90 sulphate, 1st series	Oral	2	70	20	38·1
90 sulphate, 2nd series	Oral	2	89	84–86	94–97
120 sulphate . .	Oral	2	15	9	60
30 bihydrochloride .	Intramuscular	12	30	26	86·6

[1] J. W. W. STEPHENS and others, 1918–19: "Studies in the Treatment of Malaria," *Annals of Trop. Med. and Paras.*, Vol. XI, p. 423, Vol. XIII, p. 125 *et seq.*

such thorough treatment from the beginning the tendency to relapse and latency is prevented; in other words, the disease is cured and the blood is completely sterilised as regards malaria parasites.

This course is rather drastic, but there has been a tendency during the last ten years or so to give comparatively large doses of quinine in the treatment of the initial paroxysms, not only for their greater immediate value in abrogating these, but for preventing relapses. It is never necessary to continue the use of 30–40 grains of quinine daily for longer than a week or ten days at the outside, whether we are treating a primary infection or a relapse. The administration of 30 grains daily for a period of three weeks was the treatment adopted in the malaria wards of many British station hospitals in the Northern Command in India in the later stages of the Great War. The relapse rate was 6·5 per cent. The writer has never seen or heard of better results in India or elsewhere. This success was obtained, however, at very great cost to the patient; his digestive system was upset, the anæmia continued, and his convalescence was decidedly prolonged. Many medical officers considered that this long-continued use of large doses seriously interfered with normal metabolism and the blood-making arrangements.

Regarding large doses, Sir RONALD ROSS[1] points out that the organism subjected to them appears, so to speak, to sense the risk of poisoning, and throws them out with increased rapidity, so that the amount of quinine actually circulating is lessened, not increased, by toxic doses; the total beneficial effect may then be less than with moderate doses made more use of. Similarly in the case of the development of resistance to quinine such as the brothers SERGENT have reported.[2] Ross considers that it is probably evidence of an excessively rapid excretion of quinine or its metabolite by the host, rather than of a tolerance to the drug developed by the parasite.

B. Mayne's[3] standard course.—This quinine course is easily remembered; it is something similar to the writer's, but is continued for seventy-five days only. It is as follows:

40 grains of quinine sulphate for	5 days	= 200 grains
20 ,, ,, ,,	10 ,,	= 200 ,,
10 ,, ,, ,,	20 ,,	= 200 ,,
5 ,, ,, ,,	40 ,,	= 200 ,,

—a total of 800 grains in the full course. MAYNE considers this definitely curative of malaria; it would be so in India in initial infections in the absence of re-infection.

Any one of these methods will be successful in eradicating parasites from the great majority of cases in India if the drug is actually taken and absorbed and re-infection prevented. This has been proved by the use of similar courses in cases of severe infection sent for treatment to non-malarial hill stations, though it must be said that the hill climate is a most important factor in the cure. During the War cases relapsed but little 6 miles from Edinburgh—enjoying country life, fresh vegetables, milk, good air—while in Liverpool they relapsed indefinitely. The more vigorously the quinine is given (within the limits of the tolerable) in the early stage, the fewer the gametocytes formed subsequently; there are exceptions to this rule, but it holds good for all classes of gametes, including crescents.

Experience with malaria deliberately induced in general paralytics by-

[1] *British Medical Journal*, January 2, 1921, p. 1.
[2] *Trop. Dis. Bull.*, 1921, Vol. 18, p. 96.
[3] *Journal of the American Medical Association*, 1922, II, p. 1119.

Proper quinine treatment is, therefore, one of our most potent preventive measures. The earlier and the more thoroughly quinine treatment is undertaken the fewer the gametocytes that will be formed.

A person who has had an attack of malaria, and has been properly treated by quinine during the period of the paroxysms and subsequently, should, in the absence of re-infections, be quite rid of it; that is, he should present a well-defined history of infection, paroxysms, treatment, prevention of relapses, freedom from paroxysms and return to health. Few show this clean-cut history. When it is absent, if there are no complications or other coexisting diseases, and *if re-infection is excluded,* the writer ventures to say that in the vast majority of cases there has been something wrong in the quinine treatment adopted.

With persistent relapses intramuscular injection of 15 grains of the bihydrochloride of quinine daily for three or four days is a valuable auxiliary line of treatment. These intramuscular injections often, but not invariably, break the relapses altogether, and the infection comes to an end.

For over a quarter of a century the writer has attempted to emphasise that there is a direct relationship between the duration of the infection and the efficacy of quinine treatment. He would again urge this point. This has in late years been abundantly proved by the ease with which primary induced malaria in general paralytics is cured. But it is most desirable that we should endeavour to ascertain why a recent infection is so easily cured and a chronic infection may be so intractable. It is suggested that possibly the parasites get into the spleen sinuses; once there nothing short of a bomb would get them out, for the sinus structure is so intricate that the ordinary blood current seems to flow alongside, not through, hence no quinine reaches them. Exercise may cause the spleen to eject its reserve blood.

The evidence produced here shows that we do not possess sufficient knowledge of the action of quinine in malaria to guide us as to the best way of administering the drug to bring about a permanent cure of the disease in the shortest possible time. We do not know the amount of quinine necessary to bring about disinfection of the blood, the best size of the dose and intervals between the doses, or the length of time to carry on the treatment. Many dogmatic assertions are made on these points, but they are chiefly personal opinions based on uncontrolled experience, and have not the stamp of scientific accuracy. We merely follow the methods that seem to have given us the best results without knowing how those results are achieved. From all that has been stated regarding the pharmacology, pharmacodynamics, methods of administration, action on parasites of quinine, and the administration of the drug in the malarial group of diseases, it will be recognised that many complex problems are included.

We can now state incontrovertibly that in the absence of re-infection a given dosage of quinine will cure a definite percentage of relapsing cases, and that its repetition in the relapses will cure the same percentage of these; "we have an empirical and probably correct estimate that for these relapsing cases a treatment of 10 to 15 grains daily over a period of eight weeks will cure about 90 per cent. of them, irrespective apparently of the species of parasite." The writer would like to emphasise that this applies to ordinary endemic malaria in India, and not to the relapses of epidemic malaria, which are more difficult to cure. Relapses, parasitic or clinical, must be treated as fresh infections. On the disappearance of parasites they should begin their long course again.

In relapsing cases all predisposing causes should be avoided—especially inclement weather, undue exposure to the sun, great fatigue, excesses of all kinds—any condition that decreases general bodily resistance or lowers the

Usually, whatever treatment was adopted the vast majority of benign tertian cases relapsed within a month or a month and a half after cessation of a two months' course of quinine; hence the time limit for courses of treatment should be extended to at least three months. Malaria is emphatically a disease of relapses, which may continue for months or years, without any question of re-infection, and in spite of the methods of quinine treatment adopted at the present day.

Course of quinine to prevent relapses.—When the paroxysms have ceased, a method of quinine after-treatment has to be adopted to prevent relapses. There are over a dozen ways recommended, the majority of which agree that the course should extend over a period of two or three months; some of these are referred to under STANDARD QUININE TREATMENTS, pp. 272–276. It is likewise generally agreed that 10 grains of quinine should be given *t.d.s.* for three, four or five days after the paroxysms have stopped, and before the long course is commenced. This long course may consist of:

1. 10 grains of quinine daily, the dose to be given two hours before the time the previous paroxysms used to begin.
2. 15 grains of quinine on two consecutive days weekly, say Saturday and Sunday, to be given in a single dose in the same relation to the previous paroxysms, as in 1.
3. 15 grains of quinine once a week, say every Sunday.
4. 30 grains of quinine once a week in two or four doses, say every Sunday.

Cure effected by quinine is, as noted, looked upon as a fractional process, a certain and definite proportion of each new cycle of parasites being destroyed by each course of treatment. Provided sufficient has been given and absorbed, the efficacy of quinine is considered as dependent upon the number of parasites present and the rate of their destruction, while its failure is explained as a question of relative accessibility.

Individuality of the patient.—This appears to be the dominant factor determining whether a relapse will occur, and if it does, the time of its occurrence. Referring to his and MACFIE's cases of induced malaria, WARRINGTON YORKE[1] states: "In records relating to therapy so much attention is usually paid to questions of dosage and methods of administration of drugs and to speculations regarding difference of virulence of strains of parasites, that this factor, which is seen to be of such obvious importance in governing relapses in the present series of cases, is frequently overlooked or ignored; and failure to take it into account gives rise to incorrect interpretations and deductions. This individual difference of the host, which is so essential a factor in determining a cure or in influencing the relapse period, is itself doubtless dependent on a number of conditions. . . ."

It is probable that the question of individual resistance has not so far been given due allowance in connexion with the ease or otherwise with which malarial infection is acquired. If this be true the factor of individual resistance plays a part in the quinine treatment of malaria. This latter, it would appear, includes more than finding out the best dosage, the most potent preparation, and the most appropriate time for giving the drug.

Some general considerations.—Infective persons are those whose peripheral blood contains mature gametocytes. To disinfect them these sexual forms have to be destroyed or prevented from forming. No drug except plasmochin (pp. 240, 241) has been found to remove crescents directly. But complete quinine treatment, especially in an early stage of the paroxysms, to a large extent prevents schizogonic parasites developing into gametocytes.

[1] *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XIX, No. 3, p. 116.

colour by hygroscopic action, are covered with an under-coat impervious to water.

Adulterated quinine is often sold in bazaars. The writer was told by two medical storekeepers that specimens of quinine they purchased in the bazaars contained in one case less than 25 per cent., and in another less than 40 per cent., of the base. The stock quinine mixture of the hospital is sometimes made up with less than half the quantity of quinine laid down in the hospital formulary; the balance is often stolen and sold. There have been discovered, in Bengal, tablet "factories" turning out spurious tablets of quinine which contained ¼ of a grain each (in one case none at all), although reputed to contain from 3 to 5 grains.

Again, for such reasons as prejudice, dislike of the taste of quinine, or from the deliberate intention that continuance of malaria shall ensure invaliding, the patient himself may deceive, so that in these or other ways he may fail to receive, at least in absorbable form, the amount of quinine which has been prescribed for him.

Since of quinine absorbed a moiety alone is excreted, and since a fraction is probably always excreted, in the urine, examination of the urine for quinine is a valuable check upon quinine administration. This test is carried out as follows.

If the urine of a patient taking 10 grains of quinine sulphate or cinchona febrifuge twice a day, be tested by adding a few drops of the TANRET-MAYER *reagent*[1] to 5 c.c. of urine in a test tube a turbidity occurs, and a precipitate falls if quinine is present. The urine should be acidified, boiled to free it from albumin and filtered, as the TANRET-MAYER reagent precipitates proteins; then, if no distinct turbidity appears, the patient has not taken quinine. The urines from a ward containing twenty patients can be tested in this way in a short time. It is recommended that this should be done in hospitals as a routine matter for patients taking quinine. If a negative reaction occurs in a patient supposed to be taking quinine, let the physician give the quinine himself and four or five hours later test the urine again; the result will be positive.

Another simple test for quinine in urine is that of adding a few drops of 1 per cent. picric acid solution to cooled filtered urine. A cloudy, thin, diffuse opacity appears, disappearing on heating and reappearing on cooling, whereas a precipitate of albumin increases on heating and falls on standing. Even 3 grains of quinine taken an hour before it is used responds to this test.

In hospitals a roster of all patients on quinine should be kept in the malaria wards, the amount of each dose should be entered opposite the patient's name, and the hour of administration. The drug should always be administered by some responsible person, who should satisfy himself that it has been swallowed. Moreover, in cases of doubt the practitioner need not rely only upon excretion of quinine; he can check absorption more directly, as FLETCHER points out, by giving the drug in solution and making the suspect talk to him immediately afterwards. By such simple means FLETCHER has shown that all but one of the many cases of so-called *quinine fastness* which he has investigated have yielded to quinine when there has been assurance that it has been taken and absorbed. So, too, WARRINGTON YORKE and MACFIE. The high percentage of malaria cures following the intramuscular use of quinine, after oral administration is supposed to have failed, is in part at least due to the quinine not having been taken previously. Still, it is known to most tropical practitioners

[1] The TANRET-MAYER reagent is prepared by dissolving 1·35 grammes of mercuric chloride in 75 c.c. of water and 5 grammes of potassium iodide in 20 c.c. of water and mixing them in a 100 c.c. measuring flask. The mercuric solution is poured into the iodine solution under agitation and water added to the 100 c.c. mark.

general health. If such a state exists, or if, in spite of persistent treatment, relapses continue, transfer to a healthier locality, especially to a non-malarial hill station, should be advised.

A STUDY OF THE QUESTION OF THE FAILURE OF QUININE TO CURE MALARIA

After the War there was a widespread denunciation of quinine in malaria. It was declared to be a much overrated drug, that it often failed to effect an *immediate* cure of paroxysms, and a permanent cure in a high percentage of cases; especially in those who were run down by hardship and prolonged physical strain.

The outcry against the drug in the medical journals was transferred to the lay press, the reputation of quinine was seriously injured, antipathy to it was engendered, and much suffering resulted from this loss of faith. Before going into the matter in detail, it may be stated that the following extract from the *Indian Medical Gazette*, 1921, echoes the opinion of medical men who have had much to do with the treatment of malaria in India: "What can be claimed for quinine is that, if properly used, it will rapidly relieve the symptoms due to malarial parasites, and if properly followed up, it will prevent the parasites from causing death or serious damage to the patient. . . . It is criminal to do anything to deter the patient from using this life- and health-saving remedy." It may be added that the disfavour into which quinine fell during the War was mainly due to its failure to prevent relapses of benign tertian. But as previously stated, quinine has its limitations, which were not then understood; this ignorance was responsible for the reaction against quinine therapy.

What is meant by "cure" in malaria.—The word "cure" has been used to include both complete disinfestation and a disappearance of symptoms which may be but temporary.

Causes of so-called failure in quinine therapy of malaria.—Quinine fails in malaria from many causes, a few of which are—adulteration; faulty preparation; inefficient digestion, absorption and assimilation from vomiting, constipation, diarrhœa (which may be caused by the drug itself or by parasites invading the mucous lining of the alimentary tract), or other diseases, such as enteric and ankylostomiasis, complicating the case; the use of small and insufficient doses given over long periods; lowered natural resistance due to unfavourable conditions of life leading possibly to absence or diminution of some as yet unknown protective substances against parasites or their toxins in the blood or elsewhere in the body; the locking up of parasites in regions of the body inaccessible to quinine (pp. 209, 278), especially in the capillaries of certain internal organs.

Before it is possible to determine the value of quinine or its allies in producing disinfestation in malaria, it is necessary to ascertain:

(*a*) That the disease is malaria. No reputed failure of quinine to eradicate malaria can be accepted unless microscopic examination has shown that malaria parasites have actually been present.

(*b*) That quinine has actually been taken in adequate quantities, a matter which involves the consideration of quinine resistance.

Moreover, quinine is a valuable and marketable drug and the stock solutions in hospitals do not necessarily contain the full quantity of quinine which has been drawn from store on their account. Further, certain quinine tablets have been made up with a basis which is, or acts as, concrete, so that the drug is imprisoned and unabsorbable, while others, to prevent deterioration of

And so the position is reduced to that enunciated by LAVERAN many years ago. He stated[1]: "If quinine be given in adequate doses properly administered, the diagnosis is at fault if the fever does not yield by the fourth day." As an *Indian Medical Gazette* (1921) editorial shrewdly remarks: "Those who are particularly anxious to investigate cases of malaria resistant to quinine, usually have the greatest difficulty in finding cases to investigate."

Question of quinine-fast malaria parasites.—An argument of late years advanced against quinine is that, although it controls the early paroxysms of an infection, the parasites of malaria gradually become resistant and at length are unaffected by it. The writer is disposed to doubt this form of resistance. Anyhow, the evidence that quinine-fast parasites are sometimes created by the prolonged use of quinine, when given either curatively or prophylactically, is far from convincing, and the idea conflicts with his personal experience. ACTON and his colleagues of the Dagshai Malaria Hospital state: "The parasites do not become quinine-resistant; *they disappear from the peripheral blood in as short a time with the fifth relapse as with the first.*" (The writer has italicised this very important remark.) "We have never come across a case in which the malignant or benign tertian parasite appeared to be absolutely resistant to quinine." Indeed, it is now generally accepted that after each relapse there is the same chance of cure under quinine treatment as there was after the first series of relapse paroxysms. Quinine fastness, or the resistance of a particular strain of parasites to quinine, cannot, then, be accepted as an explanation of the failure of this drug to disinfect.

WARRINGTON YORKE and MACFIE (1924), Sir RONALD ROSS and THOMSON (1917), MACGILCHRIST (1915), ACTON, CURJEL and DAVEY (1921), C. C. BASS (1923) and SINTON (1925), in several series of observations, have seen no case of quinine resistance. During the War J. W. W. STEPHENS and his colleagues in Liverpool treated 900 malaria cases—each case fully recorded—without coming across a single case of quinine fastness.

The criticisms by medical officers against the use of quinine, both as a curative and prophylactic agent, have done, and are doing, a great deal of harm in India by bringing the drug into disrepute both among the educated classes and the indigenous masses. The writer cannot recall a single case of initial uncomplicated malarial fever, of whatever type, that failed to respond to quinine treatment when the disease was taken in hand in time. This remark has been made by many experienced tropical practitioners.

QUININE PROPHYLAXIS OF MALARIA IN INDIA

What is quinine prophylaxis?—Quinine prophylaxis is the regular taking and absorbing of quinine in such a manner as to prevent paroxysms of malaria, not by the quinine acting on sporozoites, but by preventing the multiplication of the parasites into which sporozoites develop; it does not prevent infection; it cures it, or restrains.

Many years anterior to the discovery of malaria parasites and of mosquitoes as carriers of malaria, quinine prophylaxis was recognized as an effective preventive. It is recorded that as long ago as 1760 the Europeans dwelling on the Guinea coast used cinchona bark powder continuously during the rainy and unhealthy seasons. Much modern experience supports this, although of late years the reputation of quinine as a prophylactic has undergone depreciation, and it has in many quarters been condemned, mainly owing to the unsatisfactory results it yielded during the Great War. The writer cannot join in this

[1] *Paludism*, p. 93.

that often in relapse cases, when quinine given by the mouth has failed for months to stop renewal of paroxysms, a few intramuscular injections of quinine bring the infection to an end.

Malaria is one of the chronic infections (see pp. 209–211). If, after the daily administration of, say, 10 grains for a month a relapse occurs, it is said to have failed. Relapse in the circumstances is a perfectly normal incident in a high percentage of cases. Quinine cannot be said to have failed until it has been continued in adequate dosage for three months, and fresh infection is excluded during that period. In mixed infections of malignant and benign tertian parasite in India, the quinine after-treatment should ordinarily be continued for four months.

Having established then, first, that the disease is malaria, and second, that the quinine is actually being taken by the patient in prescribed doses, the way is clear to consider the reasons for failure to disinfect.

Quinine may not be absorbed. For instance:

A suckled infant with malarial fever is given, say, 3 or 4 grains of quinine a day. It has already a little diarrhœa, which the quinine aggravates; very little quinine is being absorbed. Give the nursing mother full doses for a few days and the paroxysms in the child cease. In some outbreaks of malaria, stomach and intestinal troubles are met with in from 10 to 20 per cent. of the cases. Quinine by the mouth in such cases is usually vomited, and per rectum is not likely to do much good. Half a dozen intramuscular injections stop the paroxysms.

Unfavourable conditions of life, over-fatigue, poverty, defective or deficient food, unhygienic surroundings, chills from want of clothing and bedding, may each interfere with the effects of quinine. Cases of chronic malaria on quinine and attending the out-patient dispensary or hospital for months without any effect on the disease, if admitted into hospital, put to bed, properly fed, and given quinine under supervision, lose their paroxysms and, maybe, are permanently cured. It is well known that starved and overworked people with chronic malaria require something more than quinine to cure them. Concomitant helminthiasis (especially ankylostomiasis and filariasis) is also a handicap to quinine treatment of malaria.

Effects of War on results of quinine treatment of malaria.—One series of factors in the War failures, left out of consideration in most reports, was the lowered vitality or decreased resistance resulting from the effects of being constantly under fire, expecting wounds or even death; a life of continuous monotony; exposure to all sorts of weather—burning sun or freezing cold; hardships and privations, including defective diet. These are absent in peace; it is unscientific to compare the results obtained from quinine in the two conditions of peace and war.

What is the explanation of failure to cure in any particular case in which malaria is established and quinine administration demonstrated?

There must first be considered the possibility of lack of absorption of the drug from the alimentary canal, which may reasonably be called in explanation where there is vomiting or diarrhœa, whether caused by the drug or not, and such complications as enteric and ankylostomiasis. It is probably in such cases that the benefits of intramuscular injection, as initiating a cure, have established themselves in many minds. Then, since the evidence suggests that it is not quinine which cures, but something produced by or through it, there come under consideration the causes which presumably prevent the formation of the curative body, such as the lowered bodily nutrition which was marked in certain areas, at least, during the Great War, and sufficiently evident in many parts of India.

endemic malaria, or where anophelism prevails, against all of which it is necessary to take 15 grains daily.

All these methods (except Koch's), properly carried out, will lessen the incidence of malarial fevers, but none of them will prevent malarial paroxysms in every person taking the drug prophylactically.

There is no satisfactory evidence that quinine resistance develops in those taking prophylactic quinine regularly.

Quinine does not act on sporozoites.—Notwithstanding statements to the effect that quinine acts on all stages of the malaria parasite in the blood, it is probable that it does not do so until after the parasite actually attacks the red blood corpuscles. Thus sporozoites are probably not affected by quinine in the blood. York and Macfie [1] have demonstrated that under experimental conditions sporozoites injected by an infected anopheline are not destroyed or harmed even when the donors are taking 30 grains of quinine daily.

Quinine not literally prophylactic but curative.—Quinine cannot be regarded literally as a *prophylactic* against malarial infection, as it does not affect the entrance of the parasite into the blood, nor does it prevent the first stages of the development of sporozoites in the blood, and it is very probable that it does not prevent these latter from infecting red blood cells. The drug acts chiefly by weakening or killing the parasite after it has infected the red cells, and at the moment when spores are set free from red cells.

We cannot lay in a reserve stock of quinine in the system ready to attack malaria parasites when they arrive. All experience indicates that this is a useless waste. Quinine administration during a pre-epidemic period is of no use as a prophylactic measure. It is best to start its use as soon as the risk of malarial infection arises.

It has been shown on a small scale that 5 grains of quinine every day reduce attacks by 20 per cent.; 10 grains daily by 56 per cent.; and 15 grains a day by 70–80 per cent. But even 15 grains daily do not always prevent malarial infection, and when infection as shown by paroxysms has occurred, larger doses may be needed. When malarial infection has already occurred, and the parasites are multiplying in the blood, it is no use giving small doses.

Some of the causes of failure of quinine prophylaxis of malaria in India.—It is probable that some at least of the reported failures of prophylactic quinine have arisen from a want of precise consideration of the several factors entering into this use of quinine. The predominating factor is the *quantity of quinine to be given*; there must be discrimination in this. When anophelism exists and an exceptionally high percentage of the insects is infected, their attacks will be many, and vast numbers of sporozoites will be inoculated daily. When there are only a few infected anophelines about, comparatively few sporozoites will reach the blood. The minimum quantity of quinine required to destroy the young forms developed from sporozoites has not been ascertained. The minimum dose of an ordinary endemic year would certainly be insufficient in an epidemic year, and in a year of high endemicity. It is probable that the season of the year also affects the dose required—that a larger dose is required in the late autumn than in early summer and midsummer.

Failure in a large number of reported groups is obviously due to the fact that heavy and widespread infection was already in existence when quinine prophylaxis was started. It was the writer's duty for years to review reports on the effects of quinine prophylaxis in troops in India; the most constant observation was that the drug was begun too late, and after the parasites had an innings of a month or more.

[1] *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XVIII, Nos. 1 and 2, 1924.

denunciation and is strongly of opinion that in both peace and war quinine prophylaxis serves to ward off a great many admissions for malaria. The war experience demonstrated definitely that quinine prophylaxis is not applicable to dispersed bodies of men unprovided with the necessary supervision to ensure that the drug is actually taken. The usual causes of its failure are connected with the dose, method of administration and amount of responsible supervision. Examination of the evidence on which diverse opinions are based reveals its generally unsatisfactory nature. The value of prophylactic quinine can be determined only when adequate controls check an adequately executed test, which is properly followed up.

What, then, is the effect of prophylactic quinine? It is, as just noted, really curative, using the word in the wide sense. A certain number of persons it will doubtless disinfest. In others it controls the multiplication of the parasites, so that disability is at a minimum and duties can be performed with reasonable efficiency; yet in such cases there is evidence sufficient for the conclusion that the cessation of quinine will be followed by frank exhibitions of malaria. In other instances the check on multiplication is insufficient to prevent the appearance of malarial attacks even while the prophylactic administration is in progress.

It is clear, then, that the "prophylactic" issue of quinine is called for when malarial persons, or persons liable to become malarial, are to be called upon for some duty which must be carried through while malaria is latent, and which will fail should acute illness develop. This factor must, at least in part, explain the success of ALLENBY's final advance in Palestine, seeing that the troops had taken prophylactic quinine while immobile and that, by the time Damascus was reached, whole units were out of action from malaria.

Methods of administering quinine prophylactically.—There are various methods of administering quinine prophylactically, and medical officers of the Army in India have unfortunately abundant opportunities of testing their value.

Koch's method.—Koch's *method* consists of what is known as the "long interval prophylaxis," by the giving of 15 to 22½ grains on two consecutive days at intervals of from eight to eleven days, usually on the tenth and eleventh days. This is a very unsafe method.

Plehn's method.—Plehn's *method* of "double prophylaxis" consists of giving 7 to 8 grains every fourth and fifth or fifth and sixth days.

Indian method.—A large number of medical officers in India now give a medium-sized dose (10 grains) twice a week on two consecutive days.

Method recommended.—While we have no positive statistics or scientific observations to guide us as to the best method of using quinine prophylactically, the writer recommends that, in stations where malaria is comparatively mild, 5 grains be given daily; where it is moderately severe, 5 grains daily for six days and 10 grains on the seventh day; and where severe or very severe, 10 grains for six days and 20 grains on the seventh day. In children 1 grain of quinine or 1½ grains of euquinine (in sweetened milk) for every three years of age daily in places with ordinary endemic malaria; a larger dose is required where the malaria is severe or epidemic. In all cases the dose should be given in the evening. So far as the writer's experience goes, there are not many endemic malarial places in India in which a 10-grain daily dose of quinine would not ward off paroxysms; in the large majority of places a 5- or 6-grain evening dose is sufficient. This does not apply to hyperendemic, or epidemic, or severe

infection, apart from any question of a quinine-resisting attribute of the parasite, it is necessary to increase the prophylactic dose of quinine. In the same way it is necessary to raise the dose where an increased amount of hardship, fatigue or any other factor lowering the resisting power of the individual is encountered.

In bodies of soldiers under prophylactic quinine there are nearly always some ambulatory cases of malaria (p. 182). It has been suggested that some of these mild cases are a direct effect of taking quinine for a long time (p. 206). The fewness of the parasites in the peripheral blood and the difficulty of finding them would appear to lend support to such a view. The writer has made extensive observations on this point and ascertained that, if we stop quinine altogether for a week or ten days, parasites will be readily found in the surface blood, and that usually within a fortnight a definite, frank malarial paroxysm will develop. If, on the other hand, we increase the daily dose the febrile symptoms disappear, will not recur, and parasites will not be found in the peripheral blood.

To keep soldiers and other communities in India even moderately free from malaria and in health during the malaria season, the quantity of quinine to be given them prophylactically must vary with the degree of severity of the local malaria. Rigid adherence to a set formula of, say, 10 grains twice a week when the severity of the malaria varies from mild endemicity to hyperendemicity accounts for many reported failures. Nor is it always taken into account that the malaria of the same town or cantonment may vary from year to year, and that the quantity of quinine required to ward off paroxysms must vary accordingly. Further, in an endemic area a prophylactic dose of quinine that will prevent paroxysms in the indigenous community with some degree of relative immunity will not be sufficient to do so in the case of non-immune fresh arrivals. This is constantly seen in military cantonments. The arrival of large batches of non-immunes may greatly intensify the malaria of the whole area. The non-immunes get infected, the percentage of anophelines infected increases, the degree of immunity in the older inhabitants is now insufficient to protect them, and the malaria in both the permanent inhabitants and the new-comers is widespread and severe. A vicious circle is established, which is only broken by the old and new residents acquiring immunity to this intensified infection, or by some unknown inhibitive new factor being introduced. The recent report of the Malaria Commission of the League of Nations lays great stress upon the production of epidemics by the introduction, through immigrants, of strains of malaria new to the inhabitants and against which they have acquired no immunity.

Quinine prophylaxis would be more effective if the blood were examined periodically to detect any parasites present. This may discover some infections nearing paroxysms and precautions would be taken to put them under curative quinine. If the parasites are easily found in more than 5 per cent. of the cases the prophylactic dose of quinine should be raised. Quinine prophylaxis should not be stopped abruptly at the end of the Anopheles' breeding season, as infected adult Anopheles will be still on the wing for weeks ; it should be continued for at least a fortnight after the breeding ceases, to destroy any parasites that have escaped. Further, it should be remembered that the malaria has to be eradicated from any masked or latent cases that have occurred.

All prophylactic quinine should be given in tablet or tabloid form or in gelatine capsules. The same applies to cinchona febrifuge. The tablets should not be too compressed. At several prophylactic quinine parades conducted by the writer, British soldiers, who had bought their own quinine tabloids or tablets from local chemists, pleaded to be allowed to take them instead of the solution. In a fair number of people 10 grains of quinine in solution will

A number of observations were made by WARRINGTON YORKE and MACFIE [1] to ascertain whether, by the administration of small daily doses of quinine for a short time before and after the inoculation of virulent malarial blood into general paralytics, it was possible to obtain a modified infection which might prove of equal value to the ordinary severe infection in the treatment of general paralysis. In eight cases to whom an oral dose of 10 grains was given for varying periods before and after inoculation the development of infection was prevented during an observation period varying from five weeks to four months. In the induced malaria produced by infected Anopheles it was found that when even small daily doses (5 grains) were continued for from two to six weeks after inoculation, protection was given, but that large doses given before inoculation failed to protect unless they were continued for a considerable time after inoculation.

Were the above series of observations to have included, say, 100 cases instead of a small number, they would have been a convincing argument in favour of the use of prophylactic quinine. The advocates of this practice have always definitely stated that we cannot anticipate malarial infection by giving quinine—it does not prevent infection, it has no effect on sporozoites. It prevents paroxysms; in other words, it destroys the parasites before they can multiply sufficiently to cause paroxysms, or keeps their numbers at a level insufficient to cause symptoms; the mechanism by which prevention is effected in the prophylactic use of quinine is identically the same as that by which cure of paroxysms is effected; we do not know what that mechanism is, but we do know that the drug, directly or indirectly, kills the parasites.

During the malaria season in endemic areas, when insufficient quinine is given to prevent paroxysms in garrisons and other collections of men living communal lives, we may be sure that in from 1·5 to 5 per cent. of the men it is only suppressing the symptoms, and that in a certain proportion of cases (probably under 1 per cent.), it is creating carriers. This is precisely what happened in Mesopotamia in 1915, and for some time later. We had to keep the men in the fighting line; some of those infected we knew to be carriers, although they did not suffer from frank paroxysms. We had not definitely ascertained the optimum prophylactic dose to keep all men free from a harmful number of parasites.[2] Possibly the humane element entered into our calculations; we could not ask the men to march and fight on poor rations and large doses of prophylactic quinine! CHRISTOPHERS and SHORTT in 1916, from an examination of 8,500 men on duty with their units in the Mesopotamia Expeditionary Force, arrived at similar conclusions.

It is stated by several authorities that some of those who habitually take small doses of quinine during the malaria season get infected and are then difficult to cure, and that such cases occasionally run on to chronic malaria. The explanation given is that the malaria parasite becomes quinine-resistant. We have little evidence in support of either of these statements. Chronic malaria rarely develops while taking prophylactic quinine, at any rate among troops who are watched too carefully for this to happen, and admitted into hospital when it threatens. When it occurs it would possibly be more accurately attributed to the patient's resistance having run down for some reason, the original cause of the first paroxysm being an insufficient prophylactic dose of quinine. The dose that prevents paroxysms in good health will not do so when the vitality is from any cause lowered. The European living in a malarious area develops immunity to malaria of a certain severity after a time, but he is actively attacked by paroxysms if the intensity of the infection he is exposed to is for any reason increased. Further, to meet a higher degree of malarial

[1] "Certain Observations on Malaria made during Treatment of General Paralysis," *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XVIII, Nos. 1 and 2, 1924.

[2] *Medical and Sanitary Report, 6th (Poona) Division (I.E.F.D.)*, 6th November, 1914, to 2nd August, 1915, by Colonel P. HEHIR, I.M.S.

or from other parts of India, Europeans, etc., as it is quite possible there may be unascertained differences between such different groups. For these and other cogent reasons the writer does not quote tables of comparative statistics of either successes or failures. Most of the reports express the opinion that on the whole it was a failure These reports do not discriminate between the methods of employing quinine for preventing relapses of old infections and preventing primary infections developing into paroxysms, and many of them indicate that the routine of administering the drug advised was not always carried out. The groups of statistics brought forward to show the advantages of quinine prophylaxis are not altogether sound or scientific, as at the commencement of the prophylactic use some at least of those taking the drug were already heavily infected with malaria.

The author has used quinine prophylactically against malarial infection in large bodies of men for many years, and it has never in his experience given rise to accident, except, in a few cases, slight indigestion, headache or deafness, all temporary and passing off in a day or so.

Rationale of quinine prophylaxis.—It cannot be stated that we have so far arrived at any definite conclusion from our Indian experience as to which is the best way of administering quinine prophylactically. Small groups of statistics have been published from various districts in which the endemicity has differed widely; the conditions under which the drug was given were not identical, the figures have usually been small, and control observations have not been made. Yet the question is one which in malarious districts could be solved without much difficulty; especially is this the case with troops, and in jails. Naturally the object in quinine prophylaxis is to achieve the desired result of preventing malarial paroxysms with the minimum expenditure of quinine given in the most practicable way. Whichever method is adopted it should be adhered to consistently. That chosen will, of course, be the one compatible with all the local conditions to be dealt with, the amount of responsible supervision that can be given, and of control over the recipients of the drug, being important factors. The plan to be adopted having been chosen, the length of time it is to be carried out is fixed and a formula of procedure as to the administration of the drug worked out.

While there is so much difference of opinion as to the best method of using quinine prophylactically, it would be well that the question be subjected to a rigid investigation. There are facilities for carrying out such an investigation in India not met with elsewhere. Endemic malarious areas should be chosen and to bodies of men in them quinine should be administered in various ways, control observations being made at the same time. Groups of statistics, amounting to at least an aggregate of 5,000 each, would decide the question once for all, with only a small margin of probable error. The conditions of each group as far as prevalence, intensity and liability to relapse, and as regards hygienic condition of the people, etc., should be as nearly identical as possible. We would then get a fairly correct record as to the relative prevalence of malarial fevers among persons taking the drug in these various ways, and those not taking it at all.

A difficulty which has sometimes to be contended with in the administration of quinine is the prejudice against it entertained by many Indians. Their antipathy to it is largely based on the theory that malarial fever is a "cold disease" and should be treated by a "cold remedy," while quinine is considered to belong to the opposite category of medicinal agents.

The rationale of the methods of administering quinine prophylactically differs. When quinine is given in *small doses* at frequent and regular intervals, the object aimed at is to keep always in the blood a certain amount of the drug, so that when malaria parasites commence multiplying after being injected by

produce a mild degree of cinchonism, which is not pleasant, especially if work in the sun has to be carried out. In a very small percentage of cases this liquid dose causes nausea, or even vomiting.

The writer is strongly of opinion that quinine prophylaxis does keep down admissions from malarial fevers, and if it does not always prevent paroxysms, it reduces the severity of the attacks and lowers the mortality. In this we have an abundance of evidence of men of the widest experience in India. A younger school has arisen that is endeavouring to show that it is futile. It is quite certain that with such data as we have before us at present it would be wrong to send an army into the field in an endemic area during the malarious season and not issue quinine prophylactically to it. The omission would be disastrous to the force.

"On the whole the evidence is distinctly in favour of the systematic employment of a dose of quinine daily as a prophylactic" (MANSON).

Some records of the last ten years have suggested that the failure of both curative and prophylactic quinine in areas of high endemicity and during epidemic malaria may be due to (1) exceptional virulence of the strains of the parasites or to greater toxicity of their toxins, or (2) to the large quantity of toxins created as the result of a multiplicity of inoculations by infected anophelines. The latter view is sufficient to account for the severity of the infections, and the larger number of sporozoites inoculated in the circumstance named for the failure of the ordinary prophylactic dose of quinine. The prophylactic dose of an ordinary endemic year would certainly be insufficient in a year of high endemicity or in an epidemic year. In bad malarial years in India in the Army we have been obliged to raise the prophylactic dose to 15 grains a day, and even then the admissions for malaria were high. In Macedonia, during the War, it was found that 30 grains a day was required during the worst period of prevalence to kill off all parasites entering the blood.

The supposed ease of the application of quinine prophylaxis as compared with the more permanent methods of screening and mosquito destruction appeals strongly to many. But it is not the facile process imagined, at any rate when applied to large bodies of men. The degree of success of quinine prophylaxis depends to a large extent on the completeness of control in the distribution of the drug. What full control really means is often only vaguely grasped. The number of recorded instances in which quinine prophylaxis has been carried out under satisfactory conditions of observation is very limited. The condition that the prophylactic issue should always be carried out in a manner so rigorous as to be beyond criticism is fundamental. In routine life in cantonments it is extremely difficult to observe this condition, and probably it would only be carried out in the presence of a severe outbreak.

The use of quinine prophylactically by the indigenous population of India deserves no attention. Millions of the poorer and uneducated classes are not only antipathetic to Western medicine, but have a strong prejudice against quinine, and object to a long course of the drug when they are apparently quite healthy.

If leaving, say for the hills or Europe, an endemic malarious place, where quinine prophylaxis has been followed, it is necessary that it should be continued for a fortnight (some authorities say for three months) after leaving the endemic area so as to give the *coup de grâce* to any lingering parasites.

The value of prophylactic quinine will only be determined when adequate controls check an adequately executed test properly followed up.

Statistics of failures or successes alone are not sufficient evidence as to the value of quinine as a prophylactic; they should state the classes of persons, whether indigenous

grains daily. We should commence before any serious infection has taken place, before parasites have increased sufficiently to threaten to cause paroxysms. The dose should be sufficient to kill off all the parasites that *invade the blood from day to day*. There is no idea of prophylactic quinine acting on sporozoites, it does not They enter the blood cells, and it is not until they become circulating trophozoites that they are affected by quinine. *Infection takes place*. Prophylactic quinine removes the infection; in one sense, therefore, quinine in malaria always acts curatively. Other things have to be seen to—general health, hygiene, quinine absorption, use of the drug in tablet form, occasional examination of the urine for quinine and so forth

As an administrative medical officer of the Army the writer has had a great deal to do with the prophylactic and curative uses of quinine. On the whole, he believes the drug is given in both these ways with as much care as is practicable (which, of course, is far from perfection) We know that some men in hospital evade their curative quinine in one way or another, and that a proportion of those at duty escape their prophylactic dose, but he doubts if it is possible to maintain continuously the rigid discipline that could prevent these evasions. He is quite convinced that quinine curatively and prophylactically used does reduce the incidence of the disease in the Army very materially, but it will never by itself achieve anything like total eradication of malaria in our troops in India—quinine alone will never be more than partially successful in reducing the malarial incidence. On the other hand, he is equally convinced that, combined with screening of barracks and well-planned anti-mosquito measures of a comprehensive kind, it will go very near to eliminating malaria in all those cantonments in which it is practised, except for those parts of the cantonments which are on the immediate confines of the civil administration, and where the latter dovetails into the cantonment.

SECTION 2 (*b*).—ECONOMIC PROBLEMS CONNECTED WITH QUININE IN INDIA

Introductory remarks. —The question of the provision of sufficient quinine, cinchona febrifuge, or other cinchona alkaloid at such a price that it can be used by the masses who suffer from malaria in India is one of the most difficult, complicated and important subjects dealt with in this volume. The prevention and treatment of malaria in India are intimately connected with this problem. We shall see that it includes several matters that are inseparably blended, *e.g.* the therapeutic value and pharmaceutical separation of the alkaloids of cinchona bark, and the cultural and economic conditions of the cinchona plant. An attempt is here made to give the main facts connected with the present position of the quinine problem.

Quinine[1] treatment cannot have seriously affected the incidence of malaria in India, seeing that not more than one-sixth or one-seventh of the cases of malaria occurring in a year are treated by it, as the following considerations show.

The average annual consumption of quinine in India is about 160,000 pounds. Of this, about 50,000 pounds are manufactured in the Government quinine factories at Mungpo (Sikkim) and Madras from bark grown in the plantations in the Himalayas and Nilghiris, or imported from Java. Private firms import about twice this amount.

Regarding the amount of quinine really required to treat the existent malaria in India. There are from 80,000,000 to 100,000,000 cases of malaria annually

[1] The term *quinine* includes cinchona febrifuge.

anophelines they are rendered harmless. In this method the minimum quantity of quinine that can effect this desirable object is used. Its weak point is the probability that the drug will be forgotten or not taken for some reason one day, and then the parasites may gain the upper hand, as when they have once got a foothold in the blood small doses may not eradicate them. Quinine does not prevent malaria parasites gaining access through bites of anophelines. Quinine, when present in the blood in sufficient quantity, simply renders malaria parasites harmless when they are injected, by preventing the early schizogonic cycles. In the *large-dose method*, that of giving large doses at intervals of some days, the object is to have the drug in the blood in such a degree of concentration that malaria parasites, should they meanwhile gain access and begin their schizogonic cycle, are quickly and easily killed; the parasites even at the end of the intervals between the doses are in such small numbers, and so easily assailed in their sporulating stages, as to be readily killed. On the whole, the object arrived at is attained in both methods in the same way.

We know, of course, that quinine is fairly rapidly eliminated from the system, and that by the end of the interval in the large- and infrequent-dose method there is none in the blood or in the body. In the small-dose method there is always a certain amount ready in the circulation—or somewhere in the body. The small-dose method is the more ideal way and simulates the form of acquired immunity, but is not, in endemic malarial places, relied on by many medical men, because from some accident the dose is not taken, and in the meanwhile infection may occur and then these small doses are insufficient to eradicate the parasite. Those who advocate the 5-grain dose daily hold that by this method quinine is always in the blood in sufficient quantity to kill any parasites reaching it, and yet not sufficiently to produce cinchonism. Further, they consider that the curative effects of quinine, when malarial fevers do occur, are not lessened from the system being accustomed to the smaller doses. It is to be remembered that the small-dose methods do not affect the occurrence of relapses; no ordinary prophylactic doses do this.

Prophylaxis by quinine is now adopted in practically all jails in India and for all troops. It is also in vogue amongst the greater number of Europeans residing in endemically malarial places. The extent of its use by the rural population is unknown, but in all probability it is exceedingly limited; even when quinine is available, few villagers will ever take the drug unless actually suffering from malarial infection.

Wherever quinine is being given prophylactically to bodies of men, its use should be rigidly controlled and it should be administered directly under the supervision of some responsible officer. The prophylactic use of quinine is not as a rule popular, and all possible forms of evasion are practised by those who dislike it. Whenever quinine is used prophylactically or curatively *it should be given regularly*, as it appears to be a well-recognised fact that when taken irregularly, especially in small doses, it, for some undetermined reason, seems to lessen the resistance of the organism to malaria. This irregular use of quinine and the effects therefrom are responsible for the statement that quinine has no influence in checking malaria, whereas it is not the fault of the quinine but the manner in which it is taken.

The cause of failure of quinine prophylaxis is usually either in the dose, the method of administration, or the want of supervision.

Summary of quinine prophylaxis.—In quinine prophylaxis we aim at killing the malaria parasite in the blood (or elsewhere in the body) directly or indirectly. We desire to use the smallest dose that will do this. The required dose will alter with the intensity of the endemicity—it may vary from 5 to 15

years in Sikkim, cinchona growers have aimed at producing, by continuous selection, barks containing as much quinine and as little of the other alkaloids as possible.

By 1861, the four chief crystallisable alkaloids—quinine, cinchonine, cinchonidine and quinidine—had, however, been isolated. In 1865 the Secretary of State for India ordered that a medical commission should be appointed in each of the presidencies to inquire into certain questions. "These commissions were appointed, not primarily for the investigation of the various alkaloids, but because it was considered very important, as affecting the commercial interests of the cinchona experiment in India, that authoritative medical decisions should be pronounced on the relative value of the cinchona alkaloids other than quinine, *viz.* cinchonine, quinidine and cinchonidine." Thus at an early stage the economic aspect of this question was realised. "This aspect of the general problem of what alkaloids or combination of alkaloids to use is now as important as ever, and although it need not be allowed to dictate or influence the actual carrying out of purely scientific or clinical research into the therapeutic value of the various alkaloids, it cannot be ignored in considering the practicability of any proposals based on the results of such researches. The Madras Presidency investigation was most thorough. The commission concluded that, beyond doubt, ordinary quinine sulphate, chemically pure quinine sulphate and quinidine sulphate *possessed equal febrifugal power*; that cinchonidine sulphate was only slightly less efficacious, and that cinchonine sulphate, though considerably inferior to the other alkaloids, was, notwithstanding, a valuable remedial agent in malarial fever."[1] The other two commissions arrived at similar conclusions. These opinions spread in the medical profession and among chemists. Official encouragement was given to the use of the other alkaloids in India. It was expected that they would remain at their relatively low price. They did not. As the quinidine and cinchonidine had been declared equal to quinine their prices soared to above quinine itself. Up to this no alkaloid had been produced in India on a commercial scale, but in 1873 the total mixed alkaloids of *Cinchona succirubra* were extracted to test their value in 1,000 cases of malaria in civil and military hospitals. "The Surgeon-General reported that it was a sure febrifuge, and if it could be sold at only 1 rupee per ounce or cheaper, that it should be manufactured in large quantities. In 1874 cinchona febrifuge began to be manufactured, and from then to 1887 was the sole product of the Indian factories. About the same time (1874) the policy of replacing *C. succirubra* on the plantations by quinine-yielding species (*C. calisaya*, *C. ledgeriana* and its hybrid with *C. succirubra*) was begun; but it was not until 1887 that it was found possible to start the manufacture of quinine in India. By that time the vast extension of cinchona cultivation in India, Java and Ceylon—which, although not in excess of the needs of the malaria-stricken, was far in excess of the arrangements for supplying those needs, and so of the actual commercial demands—had led to a tremendous fall in the price of quinine from about £1 per ounce in 1878 to less than £1 a pound in 1890."[2] The gradual lessening of the supply of *C. succirubra* bark and the fall in the price of quinine were commercial factors that greatly influenced the use of cinchona febrifuge. Further, the therapeutic efficiency being reputedly approximately equal, the presence of secondary or æsthetic qualities affected the selection of a drug; in this respect quinine had the advantage of cinchona febrifuge in those days, when neither was available in tablet form. In 1892 another factor affected the problem—the sale of quinine to the public in 5-grain packets at 1 pice each.

[1] Lt.-Col. A. T. Gage, C.I.E., I.M.S., "Cinchona Alkaloids and Malaria," in *Trans. Roy. Soc. Trop. Med. and Hyg.*, January 15, 1925, Vol. XVIII, p. 347.
[2] *Ibid.*, p. 348.

(pp. 10, 12 and App. I,[3] p. 440); of these, about 8,000,000 attend hospitals and dispensaries. Assuming that at least 110 grains of quinine are required to cure a group of paroxysms, the demand for hospitals and dispensaries should be 125,000 pounds. "Hospital patients do not get anything approaching this quantity, because the price of quinine is prohibitive. . . . The potential demand for quinine is, therefore, somewhere between 125,000 and 1,500,000 pounds."[1]

We may arrive at the quantity required in another way. "The Government of Italy, in 1903, made quinine a State industry, and thereby cheapened the retail price, enormously increased its consumption, and reduced the malaria mortality from 15,000 to less than 3,000 per annum. The consumption in Italy is about 15 grains per head of the population. Malaria is more widespread in India than in Italy, but if the population in India consumed quinine on the same scale the consumption would be 520,000 pounds. It must not be thought that such consumption would suffice for India; it could be four times this. There can, however, be no question of effective treatment of malaria in India until the consumption approximates 500,000 pounds. This quantity may be looked on as the minimum potential demand for India, and 1,500,000 pounds as the probable maximum. Now the total world output of quinine is about 1,000,000 pounds, nine-tenths of the bark from which it comes being grown in Java. It is clear that the world could not at present meet this, the Indian demand, and also that the demand will never be realised while present world prices continue."[2]

In an article on indigenous quinine production contributed to *The Pioneer* in 1910 by the writer, he estimated that the smallest quantity of quinine that could produce any decided amount of good in the general population by partial treatment *during epidemic times* was about 3,500 pounds per million of people. This fact emphasises the necessity of increasing the output of indigenous quinine and lessening its price. As cinchona trees do not yield bark for some years after being planted, it would be some time before a sufficient quantity of quinine and mixed cinchona alkaloids could be regularly manufactured, even supposing that the cinchona plantations in India were at once considerably extended.

The History of the Cinchona Alkaloids in India

Quinine was first used in India in 1826, at which time the Government of Bombay bought some for experimental use at a cost of £28 10*s*. 8*d*. per pound. It was not brought into general use in India until 1840–5. Cinchona cultivation was started in India in 1861. In 1874 a light-coloured powder consisting of the total alkaloids of the red cinchona bark was manufactured. The powder was called *Quinetum* (p. 259) or *Febrifuge*. At first a considerable proportion of *Cinchona succirubra* (which is poor in quinine but rich in quinidine, cinchonine and cinchonidine) was cultivated (Plate XV). Large sums were spent by Government and private planters on this species, but its low quinine output was a serious commercial drawback. In 1865 medical men demanded quinine because they were familiar with it, since it was the first alkaloid separated from the bark, and its efficacy was accordingly demonstrated before any knowledge of the existence or value of other alkaloids became generally known. Consequently *C. ledgeriana* (Plate XV), rich in quinine, was introduced. Quinine manufacturers and cinchona growers adapted respectively their machinery and species of cinchona cultivated to the demand, and have since continued to do so. Thus for the last half-century in Java, and for the last thirty

[1] *Report of the Public Health Commissioner with the Government of India*, 1922, Vol. I, p. 103.
[2] *Ibid.* [3] *Ibid.*, 1924.

Java appears to be the only country in the world that can make the manufacture of *quinine* really profitable. It has the climate, the volcanic soil, the altitude and rainfall in which grow most luxuriantly the species of cinchona producing the largest proportion of the quinine base, and labour is cheap. Java manufacturers have attained to a very high standard of scientific organisation in the production of quinine, resulting from over fifty years of experience. Even supposing that *C. calisaya* and its hybrids could grow equally well elsewhere, it is highly improbable that another country could produce quinine at the price at which Java can, with which country it could not, therefore, successfully compete. The monopoly acquired by Java is not a cinchona monopoly, but a quinine monopoly; it attained this position because of the reputation quinine obtained over fifty years ago, as the only alkaloid in cinchona that is a specific in malaria. This error has suppressed the cultivation of the species that yield the best cinchona febrifuge.

Large quantities of *Cinchona ledgeriana* and *C. ledgeriana* × *C. succirubra* barks are used in the Indian factories. The following are analyses of these barks grown in the Rangbi Valley, Sikkim:

CINCHONA LEDGERIANA

	Percentage in stem bark.	Proportion of the total percentage of alkaloids in stem.
Amorphous alkaloid	0·60	10·4
Cinchonine	0·25	4·3
Cinchonidine	0·36	6·2
Quinidine	0·44	7·6
Quinine	4·14	71·5
	5·79	100·0

CINCHONA (LEDGERIANA × SUCCIRUBRA)

Amorphous alkaloid	0·54	11·9
Cinchonine	0·46	10·1
Cinchonidine	0·33	7·3
Quinidine	0·34	7·5
Quinine	2·87	63·2
	4·54	100·0

"It will be seen that the total of all the alkaloids other than quinine is a little more than a quarter of the quantity of quinine in the case of *C. ledgeriana*, and only a little less than half in the case of the hybrid, and that the fraction becomes very much less if any one of the other alkaloids be taken separately. Should a demand arise for any one or more of those alkaloids separated, so long as the demand is small quinine manufacturers will be glad to get rid of those by-products, at relatively cheap rates, but if the demand should increase, the price will then start to rise, and will continue to rise until it will be equal to, or even exceed, the price of quinine. The separation of any one or more of those alkaloids would also, to the extent to which it or they would be separated, affect the production of cinchona febrifuge, either by leading to a disappearance or material reduction of one or more of its constituent alkaloids, or to a reduction in output of cinchona febrifuge of full alkaloidal content. In the former case the therapeutic value of the febrifuge might be seriously affected, in the latter case its price would almost certainly soar. So any initial support from the financial side that might seem to favour proposals, primarily based on purely clinical results, for even only a moderate replacement of quinine by any one of the other separated alkaloids,

Pervading, and more or less reinforcing, all those factors was the long-established pre-eminence of quinine in general, if not universal, medical opinion.

By 1903 the scarcity of *C. succirubra* led to an alteration in the process of manufacture of cinchona febrifuge. From that year it has consisted of the mixture of the residual alkaloids (see pp. 256, 257) remaining after the extraction of quinine from the barks of *C. ledgeriana* and its hybrid with *C. succirubra*, a certain amount of quinine being added to the mixture to make it approximately similar in composition to the original cinchona febrifuge containing the total alkaloids of *C. succirubra*.

The manufacture of cinchona febrifuge in the Mungpo factory declined from 11,000 pounds in 1881 to 1,600 pounds in 1911; in the latter year the decline in the price of quinine stopped. "In 1918 the first agreement between Java planters and the quinine manufacturers to regulate the supply of bark and the price of it and of quinine came into operation. The immediate result was a rise in the price of quinine. The enormous demands during the War accentuated the rise, and affected the demand for cinchona febrifuge to such an extent that the sale from the Bengal factory rose to 16,200 pounds in 1919. The demand exceeded the possible supply and the price had to go up."[1]

But other factors outside the control of therapeutics and laboratory are in operation. "There are a small number of patients in comfortable circumstances for whom the cost of a remedy is of no importance. There are a small number of sufferers in civil and military hospitals who also have at their service skilled attendants and may have a choice of alkaloids. But far exceeding these we see a vast multitude of human beings who live on continuous sufferance of the pestiferous mosquito, who may never see a hospital or a medical man, and to whom cinchona alkaloids are unknown, or unprocurable at a price within their scanty means. For the treatment of the first two classes the determination, as accurately as possible, of the relative therapeutic value of the various alkaloids may well be of great practical importance—provided other things are favourable—but for the great mass of malaria-stricken humanity these other conditions are likely to continue in the future, as they have done in the past, to exercise a powerful influence in deciding what alkaloid or alkaloids are to be used."[2]

Cinchona cultivation is carried out on an immense scale in Java; which, in 1920, exported 4,526 tons of cinchona bark, and 418,861 kilos of quinine, one-third of which was taken by the British. This was 200,000 kilos less than in 1919. This drop was not due to less production, but to the fact that the Quinine Manufacturers' Association was holding up the stocks to prevent a fall in price. It is unnecessary to comment on this regrettable state of affairs so far as the supply of bark products to the suffering masses of India is concerned. A widespread fallacy exists to the effect that there is a quinine shortage in the world. This is not the case. There is such an enormous surplus of bark that cinchona planters have been compelled to limit the output. Production exceeds consumption. But more quinine is not produced than is demanded for the treatment of the malaria cases of the world; the price of quinine places it beyond the reach of the millions who suffer from the disease; the masses cannot buy it; no Government can provide it for them. The production of quinine during the three years 1921–3 was 1,583,000 kilos, but the consumption was only 1,224,000 kilos. In 1922 there were 218,923 kilos less bark harvested than in 1921.[3]

[1] Lt.-Col. A. T. Gage, C.I.E., I.M.S., "Cinchona Alkaloids and Malaria," in *Trans. Roy Soc. Trop. Med. and Hyg*, January 15, 1925, p 349.

[2] *Ibid.*

[3] *Chininum*, 1923.

composition, this varying with every batch of bark used; no two samples are identical. It is not standardised. Moreover, there is nothing to prevent anyone fraudulently selling anything as cinchona febrifuge.

The position that quinine has attained as the best of all the separated alkaloids for the widest use seems unassailable, and is likely to remain so for years to come. But quinine might easily be supplemented by a properly controlled cinchona febrifuge. This could be done easily, cheaply and abundantly by reverting to the cultivation of *C. succirubra* and the extraction of the total alkaloids to form again the original cinchona febrifuge. *C. succirubra* is a robust species, yielding considerably more bark than the other species, and with a reasonably high average percentage of total alkaloids. As the latter would not require to be separated, the preparation of cinchona febrifuge would be a comparatively easy and cheap process.[1]

It will be observed that the whole subject is highly technical, but without a full comprehension of the intricacies of the problem it is not possible to form a definite, sound and business-like opinion upon it. The writer has taken the liberty of giving Lt.-Col. A. T. GAGE's own words *in extenso*, apprehending that any abridgment might lead to absence of clearness. Lt.-Col. GAGE's remarks were endorsed by Sir DAVID PRAIN, I.M.S. We have, therefore, before us the reasoned opinions of the two greatest living authorities on this vital question as it affects malaria in India.

Manufacture of the alkaloids of cinchona bark in India.—A brief reference to this subject may elucidate some of the foregoing statements. In general terms the separation of the alkaloids of cinchona bark was originally effected by making an acid infusion of the bark. This infusion was treated in one of two ways. If the bark's quinine content were not sufficiently great to permit economically of the commercial extraction of quinine, the whole of the alkaloids were precipitated therefrom by caustic soda and sold as *cinchona febrifuge*. If, however, the bark's quinine content were high, the sulphate was separated from the acid infusion by special means.

After extraction of quinine the infusion may again be treated in one of two ways. Either the whole of the *residual alkaloids* may be precipitated by caustic soda and used for treatment (and it is this residual alkaloid which has latterly been sold as cinchona febrifuge), or there may be extracted, one by one, first the crystalline alkaloids by precipitation (*cinchonidine* as a tartrate, *quinidine* as an acid tartrate, and *cinchonine* by virtue of its insolubility in 80 per cent. alcohol), then the non-crystalline as a brittle or treacly mass, thrown down by the evaporation of the spirit in which they have been dissolved and known as *quinoidine* or *amorphous alkaloid*.

If it can be shown beyond all controversy that cinchona febrifuge is even approximately equal to quinine therapeutically in malaria, the main difficulty connected with this problem will be solved (see p 257). Then a consistent policy of increasing the number of *C. succirubra* plants under cultivation as the demands for cinchona febrifuge rise would be indicated. But medical opinion on this subject has not been stable; it is less so to-day than it was fifty years ago. Until it has reached stability it is impossible to formulate a new policy of cinchona planting that will reduce both the price of quinine and of the other alkaloids. At the present time scientific inquiry is taking place in testing the therapeutic value of cinchona febrifuge in malaria, using quinine sulphate as a control. This investigation should be completed in a few years.

Five series of experiments conducted at widely different times (Bengal

[1] Lt.-Col. A. T GAGE, C.I.E., I.M.S., "Cinchona Alkaloids and Malaria," in *Trans. Roy. Soc. Trop. Med. and Hyg.*, January 15, 1925, p. 352.

would, under existing cultural and commercial conditions, soon disappear. The replacement of quinine by any other alkaloids would be inseparable from grave cultural and commercial consequences. The amount of any one of the other alkaloids in the barks under cultivation is so relatively small that at least five times as much bark and chemicals in proportion would be required to produce a quantity of alkaloid equivalent to the quinine it was intended to replace, and, in consequence, the cost of production would much exceed that of quinine—which would tend to become a by-product, and one of far more abundance than the main product, and relatively so much cheaper than the main product as to be preferred, in all probability, by the majority of sufferers who could not afford the other."[1]

It is, of course, possible that some of the other species of bark may, by selection of trees for seed, be made to yield a larger percentage of any special alkaloid, other than quinine, just as *C. ledgeriana* has been made to secrete an increased average percentage of quinine. But quinine is not an annual crop. "During the years—and they would not be few—over which the trees would be in training to secrete the clinically desired alkaloid in the commercially desired amount, it may be doubted whether happy expectation would correctly describe the condition either of the cinchona industry or of the medical profession or of the malaria-ridden."[2] The stripping of the better classes of bark is now not commenced until the tree is eight years old (see p. 252).

The alkaloids of cinchona bark are either crystalline or amorphous. Regarding the crystalline alkaloids see pp. 255–258. The amorphous alkaloids are grouped under the name *quinoidine*, which in effective doses against malaria parasites appears by FLETCHER's experience to be toxic to man, giving rise to vomiting and diarrhœa (pp. 258, 259). The chemical relations of the amorphous to the crystallisable alkaloids are less clear than the interrelationship of the crystallisable, whose remedial powers are believed to differ. The relative proportion of these alkaloids in particular kinds of cinchona remains unaffected by the variation in the total. In any sample of the red bark half of the alkaloid is cinchonine, one-third quinine, one-sixteenth cinchonidine, only one-eightieth quinidine; the remainder, about one-eighth, is amorphous. But the relative proportions of these alkaloids vary in different kinds of cinchona bark. In red bark quinine forms about one-third of the alkaloid content, in crown bark it forms three-fourths. In yellow bark the proportion of quinine is higher than in crown; in the grey bark the proportion is lower than in red.

Control of some kind is essential. Regarding legal control there are difficulties. For instance, the quantitative analysis of a batch of cinchona febrifuge occupies many days and is correspondingly costly, and should it be enjoined that the package must have printed on it the composition of its contents, the cost of analysis will exclude from the market all small-scale preparations. FLETCHER's suggestion to overcome this difficulty is that the sale of febrifuge should be a strict Government monopoly, that a large batch, purchased or manufactured, should be mixed thoroughly and analysed, and that every package on sale should bear the composition as thus ascertained. It would seem that the proportion of amorphous alkaloid must be kept as low as possible.

Quinine and cinchona febrifuge compared.—Quinine tablets have certain advantages, some of them æsthetic, over those of cinchona febrifuge. Quinine is a white salt and the public prefers spotlessly white quinine tablets to the spotted brownish ones of the febrifuge. Quinine is a definite, invariable chemical compound. Quite apart from fraud, cinchona febrifuge is of inconstant

[1] Lt.-Col. A. T. GAGE, C.I.E., I.M.S., "Cinchona Alkaloids and Malaria," in *Trans. Roy. Soc. Trop. Med. and Hyg.*, January 15, 1925, p. 351.
[2] *Ibid.*, p. 349.

the least possible cost, can be distributed at the least possible price, and can be used with the least possible medical supervision."[1] For some years to come, quinine only will be available indigenously in India, supplemented by the new form of cinchona febrifuge referred to on p. 256.

The price of quinine and cinchona febrifuge should be kept within reasonable bounds. This can only be done by the Central Government, or Provincial Governments, owning the cinchona plantations, manufacturing the drugs, and regulating their sale and distribution in the country, or contracting with private owners of plantations for the provision of the bark at stable rates. The incidence of malaria in India varies from being, in dry years, mildly endemic, with a low demand for these drugs, to being, in years of floods and heavy rains, highly endemic over widespread areas, or even epidemic, with high incidence and mortality and a heavy demand for these drugs. In existing circumstances, in the former case the price of quinine and cinchona alkaloid is roughly a rupee an ounce, in bad malaria years it soars to Rs.15 or more an ounce, and is then not within the means of the masses (who require these drugs most) to purchase. A similar rise in price happens in practically every war of any dimensions. What can be done by this central control of the price of quinine has been practically demonstrated by the Italian Government. In 1903 they centralised the manufacture and issue of quinine products, with the result shown in the following Table.

Quantity of Quinine sold by the State in Italy

Year 1902 . .	1,313,730 kilos	Year 1906 . .	19,512,404 kilos
,, 1903[2] . .	4,166,855 ,,	,, 1907 .	22,214,616 ,,
,, 1904 . .	10,663,910 ,,	,, 1908 . .	24,138,820 ,,
,, 1905 . .	16,318,877 ,,		

There is considerable profit in the whole enterprise, and this profit in Italy is ear-marked for anti-malarial measures.[3]

One of the points at which the links of the epidemiological chain of malaria can be severed is the sick man suffering from malarial infection. But how are we to get at him? Not more than 15 per cent. of the cases of malarial fever in India come under quinine treatment. Charitable and travelling dispensaries open a way to increase this percentage. They should be multiplied at least fivefold throughout the country. Once a sufficient number are established they should work automatically. The first stages of this work only should be organised and carried out by the Provincial Governments; the later stages should be carried out by the people themselves. The first stages should be largely educational and aim at popularising the early treatment of malaria by quinine, and teaching the people how to carry out anti-anopheline measures. Among the better classes of Europeans and Indians pronounced cases of malarial fever are now treated by quinine much sooner, much more energetically, and for a much longer period than was formerly the case, with considerable success. In Italy, once charitable dispensaries were properly established, the treatment of malaria advanced by leaps and bounds. The writer would point out, however, that it would be unwise to create suddenly a demand for enormous quantities of quinine and cinchona alkaloid until that demand can be met at a price that can be paid by the masses of India. The anti-malarial laws

[1] Lt.-Col A. T. Gage, C.I.E., I.M.S., "Cinchona Alkaloids and Malaria," in *Trans Roy. Soc Trop Med and Hyg*, January 15, 1925, p. 351.

[2] State control of quinine began. Commencement of general use of quinine in endemic malarious areas, application of laws against malaria.

[3] *Annual Report of the Public Health Commissioner with the Government of India* for the year 1922, Vol. I, p. 82

Government, 1873; Lt.-Col. A. C. MacGilchrist, I.M.S., 1910–12; Major W. H. Acton and colleagues, 1918; Dr. W. Fletcher and colleagues, Federated Malay States, 1922–3; and Dr. W. Fletcher again in 1925) seem to show that cinchona febrifuge is in general terms as useful in the treatment of malaria as the officinal alkaloid quinine. The last series of observations on the value of cinchona febrifuge in malaria were conducted under rigid scientific conditions by Dr. W. Fletcher. He states "The *sample of cinchona febrifuge* was as efficient as quinine in doses of 10 grains twice a day" in male adults. There are, however, serious differences of opinion in the details of these reports, especially as regards the effects of the individual alkaloids contained in cinchona febrifuge. The impression left after carefully reviewing these reports is that the pharmacology and therapeutics of cinchona febrifuge have not as yet been sufficiently worked out. The differences of opinion referred to may possibly be due to variation in the composition of the cinchona febrifuge used by the several investigators. Until the total alkaloidal content (cinchona febrifuge) is standardised no uniform results are possible.

The variations in composition, of cinchona febrifuge obtained from a number of different sources, are shown in the accompanying Table by Mr. Bernard Howard.[1]

	1.	2	3	4	5	6	7	8	
	Dr Vrij's Analysis of Java Febrifuge, 1876	MacGilchrist's Formula, 1915	Composition calculated from Hooper's Bark analysis	Indian Govt Tablets, 1913	Febrifuge from I G Madras Factory, 1923	I G. Febrifuge, 1922, quoted by Lt.-Col. Gage	B.K.F. make analysed for Dr Dale, 12-2-24	B.F.K. make from India, 7-3-22	Average contents of Bark worked at Howards' Factory, mainly Java Ledgeriana, 1919-1923
Quinine Alkaloid	2·9–22·2	7·40	24·0	2·7	8·0	10·5	5·8	11·0	4·143
Cinchonidine ,,	24·0–60·4	5·84	28·0	3·4	21·0	7·0	12·2	9·2	0·512
Cinchonine ,,	18·0–54·0	16·58	15·0	12·3	21·0	23·0	20·0	15·3	0·381
Quinidine ,,	2·8–5·4	23·83	8·0	12·5	4·5	16·0	8·7	4·8	0·170
Amorphous ,,	0·4–21·0	29·12	25·0	54·9	30·0	33·0	41·3	45·4	0·888
Ash, Moisture, etc.		16·12		14·1		10·5	3·7		
		98·80		99·0		100·0			6·134

To sum up, the question of the therapeutic efficacy of cinchona febrifuge in the treatment of malaria is of world-wide importance. Cinchona febrifuge can be manufactured from hardier species of the cinchona plant that are less selective as regards the conditions in which they grow than are the species with high quinine content, and that could be cultivated in many parts of the world. It is no exaggeration to state that the solution of the problem under discussion in India is the manufacture of cinchona febrifuge on a large scale from *C. succirubra*, if it can be definitely shown that this preparation is as good, or nearly as good, as quinine in the treatment of malaria.

Attention is specially called to the following words from Lt.-Col. A. T. Gage's address; they embrace the main point of the problem under consideration: "Until it is accepted beyond all doubt that one particular alkaloid, or combination of alkaloids, is so far superior to any others in the treatment of attacks (of any kind of malaria) as to exclude consideration of the others, then the fittest alkaloid, or combination of alkaloids, for the overwhelming mass of sufferers will be that which can be produced in the greatest abundance at

[1] *Proceedings of the Roy Soc. Trop Med. and Hyg.*, January 15, 1925, p 358.

and a state of education in sanitation which all classes of the Indian community do not possess.

Screening of houses, in India, is on the whole one of the cheapest general methods of preventing malarial infection through anophelines. It is indicated where anti-larval measures are inadequate, and is specially applicable to private dwellings, since it renders the occupants independent of their neighbours' neglect. It is used to but a limited extent in India. There are many thousands of "inspection" bungalows all over the country, in malarious districts, in which there is no other practical method of preventing the attacks of mosquitoes. All barracks, hospitals and official quarters in malarious districts should be provided with wire-gauze protection.

Tinned wire gauze is useful and inexpensive. Plain iron gauze soon rusts and becomes useless, especially during the rains and near the sea. Copper or brass gauze is very durable, but nearly twice the price of tinned wire. The wire gauze known as *screen cloth* (see p. 305) is now very largely used. The best metal for screen cloth is the non-corrosive but rather expensive monel metal.[1] Torn wire screen is repairable by placing a small piece of screening over the tear and sewing it firmly with a strand of thin wire.

For houses of poor construction or in bad condition efficient screening is impracticable. Badly constructed, improperly fitted or too coarse screens are dangerous, as are sliding screens, which are sometimes negligently left open. Of the numerous screened buildings which the writer has inspected, in less than 40 per cent. were they keeping out all mosquitoes. No mosquitoes are to be found in a well-screened house, even when they are present in swarms outside. A badly screened house is a mosquito trap, and is perhaps worse than an unscreened dwelling.

In the screened house all indispensable exterior doors are self-closing and fitted with wire gauze, and other openings are permanently closed by frames covered with the same. Automatic closing is effected by spring-hinges, rubber bands, or weights over pulleys. Certain useful details are the following.

Screening of doors.—All mosquito-proof doors must open outwards (otherwise mosquitoes resting on the outside may be brushed into the room by persons entering) and be sufficiently far apart to permit of a person standing between them, one door closing before the other is opened. All carelessness in using the doors should be looked upon as a grave offence.

Screening of windows.—The frame of the screen must fit tightly up against the battens. A very good type of screening for windows is that in which the top of the frame is hinged to the batten over the window with small metallic fasteners. The parts of the fasteners attached to the screen frame fit into the parts on the window batten. A hook at the bottom of the screen frame, connecting with a ring in the window ledge, draws the frame of the screen tightly against the window battens on the sides and top and the ledge on the bottom. If there is no suitable batten, or when the window frame is of bad shape, it is probably best to fix the screen cloth over the whole window, using moulding strips over the tack heads around the window opening. Iron brackets should be used to strengthen the corners of the window screens.

Screened doors and windows are fixtures for the season, *i.e.* while mosquitoes are on the wing, and are thus different from complete screening, which is fixed and permanent.

Screening of fire-places and chimneys.—Unused chimneys are favourite

[1] *Monel metal* is composed of—nickel 67 per cent., copper 28, other metal 5; it is a natural alloy of metals and contains no tin, zinc or antimony.

now in force in many countries have created an excellent social prophylaxis of malaria.

Every aspect of the problem of quinine in malaria in India is associated with *serious difficulties, and it is only a right understanding of the nature of these* difficulties and a full determination to overcome them that will ensure a right solution.

Before concluding this section the writer would remark that the enormous difficulties connected with the quinine question in India would be solved by the discovery of some inexpensive way of making synthetic alkaloids to replace the *quinine alkaloids. This is a direction in which research should persistently* be carried out. Success would eventually repay a hundredfold the labour and cost of the discovery.

Section 3.—MOSQUITO CONTROL IN INDIA

This Section is considered under the following headings:

A.—Methods of Protection against Adult Mosquitoes, B.—Destruction of Mosquito Larvæ by Larvicides, etc.; C.—Destruction of Mosquito Larvæ by Fish; D.—Drainage and Regulation of Surface Waters as Anti-Mosquito Measures; E.—Methods of Draining and otherwise Dealing with Marshes and Places Simulating Marshes: F.—Filling Operations, G.—Cultivation and Arboriculture as Anti-Mosquito Measures.

A.—METHODS OF PROTECTION AGAINST ADULT MOSQUITOES IN INDIA

Under this sub-heading it is proposed to deal with:

(*a*) Mosquito-Proof Houses—Screening.

(*b*) Personal Protection by:

(i) Mosquito-Nets, (ii) Punkahs and Electric Fans; (iii) Mosquito-Proof Clothes, (iv) Culicides; (v) Culicifuges and Mosquito Repellants.

(*c*) Other Measures.

(*a*) Mosquito-Proof Houses—Screening

A considerable part of the prevention of malaria is embraced in protection from mosquito bites; complete defence in this respect would break the chain of the malaria cycle. Protection from the bites of mosquitoes by wire gauze consists in making human habitations impenetrable to mosquitoes by closing all openings with wire gauze having a mesh of about sixteen strands to the inch (p. 305).

Were *houses and huts in India properly screened*, and kept in that state, the malaria problem would be shorn of most of its difficulties and much of its terror. The public of the malarious counties of the United States pay screen-cloth manufacturers £5,000,000 a year for screening new buildings and repairing the screens in old ones. The writer's experience on a "screened" ambulance train bears this out (see p. 56). The success of this method of protection is no *longer a matter of doubt.*

Malaria has undergone marked decrease wherever screening of houses to prevent the entry of mosquitoes has been adopted. The records show a *reduction of 50 per cent. and over as compared* with unscreened houses in the same places. Screening excludes not only mosquitoes, but flies and other insects, reduces dampness and glare, and allows of some movement of air. A *mosquito-protected house* is, theoretically, an ideal method of excluding mosquitoes, but it involves a large initial outlay, subsequent care,

readily fitted. If there are electric fans in the verandah, the screened portion should include one or more of them.

Portable screened room.—Such a screened room may be placed within the bedroom, and fitted in such a way as to enclose the shaft of an electric fan. It may be permanent or made to be dismantled daily. Portable rooms of this kind are obtainable, and are specially useful for touring in malarious parts or sleeping out of doors at night. In whatever way effected the bed must be mosquito-proof.

Servants' quarters and occupied outhouses should likewise be screened; the inhabitants of these buildings are often the carriers of the malaria that reaches their employers through Anopheles

Screening of hospitals.—All hospitals, civil and military, in the plains and lower hill stations, or at least all wards containing malaria cases, should be effectively screened to prevent infection and re-infection of the malarial patients themselves, and of those who surround them, including the hospital staff. When screening cannot be carried out mosquito nets should be used, but the latter will rarely be more than a partial success. In highly organised and disciplined hospitals mosquito nets are undoubtedly of great use, but they throw much work on the hospital establishment. See Fig. 73—I, Sectional Elevation and Plan, and 73—II, Section of a screened hospital.

The following two illustrations[1] of a screened hospital are self-explanatory.

Introduction of screening into towns, cantonments, etc.—When introducing screening into cantonments, towns, "civil lines," railway stations and railway employees' quarters, and other places, all buildings to be screened should be thoroughly surveyed and divided into three groups:

(1) Those in a satisfactory state that can be screened at once.

(2) Those that can be put into such a state by certain repairs or alterations.

(3) Those that cannot be successfully screened.

The third group should not be touched. Owners of houses of the second class should be given a certain time to make the required changes. All screening should be carried out systematically and completely. Afterwards a routine monthly inspection should be made to ensure that the screening is being kept in good condition. The usefulness of screening depends on its completeness, and its longevity depends upon the skill in the workmanship, the material used, and the care it receives. All mosquito wire-gauze netting requires constant inspection, and, unfortunately, often calls for repairs.

In the absence of wire-gauze doors and windows the covering of all openings with mosquito netting or butter muslin fixed to the framework may be adopted. Muslins are manufactured in many parts of India, are very cheap, and it is possible to cover all the required doors and windows of a large house for a few rupees. They are easily repaired and replaced and offer some protection. They, however, interfere with the current of air and may make the room close, a fact which is likely to lead to their being put out of action.

(b) Personal Protection

(i) *Protection by Mosquito Netting*

Probably four-fifths of the cases of malarial infection arise from bites of malaria-carrying Anopheles between dusk and dawn. Mosquito nets, properly made and used, are next in effectiveness to screened houses in protecting against the attacks of mosquitoes. Some form of gauze material around beds to protect from mosquitoes has been in use for many centuries. ANNESLEY, in

[1] From Sir MALCOLM WATSON's *Prevention of Malaria in the Federated Malay States*, 2nd Ed., pp. 262, 263.

entrance and resting places for Anopheles, some of which even hibernate in them. Such chimneys may satisfactorily be closed by covering the top with screen cloth held in position by surrounding bricks Since its meshes are readily choked by soot, the screen must be removed when the fire-place is used. Alternatively the fire-place may be closed by a framed screen made to fit the opening exactly. In this case any stove-pipes opening into the chimney must be blocked.

Screening of ventilators.—Ventilation openings are most important.

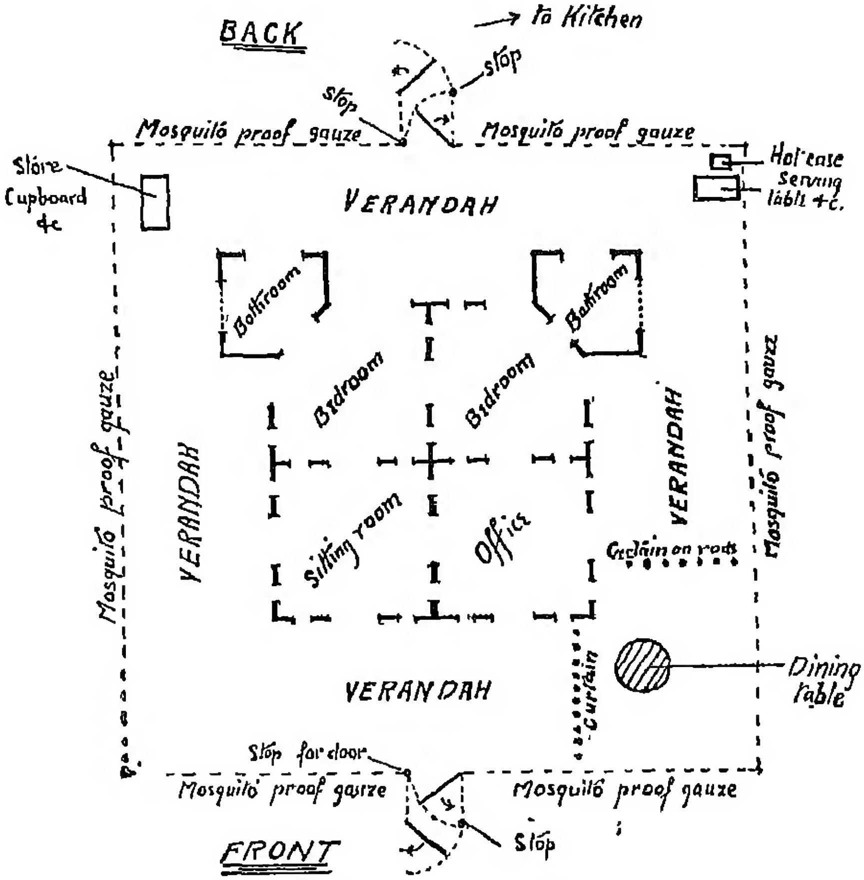


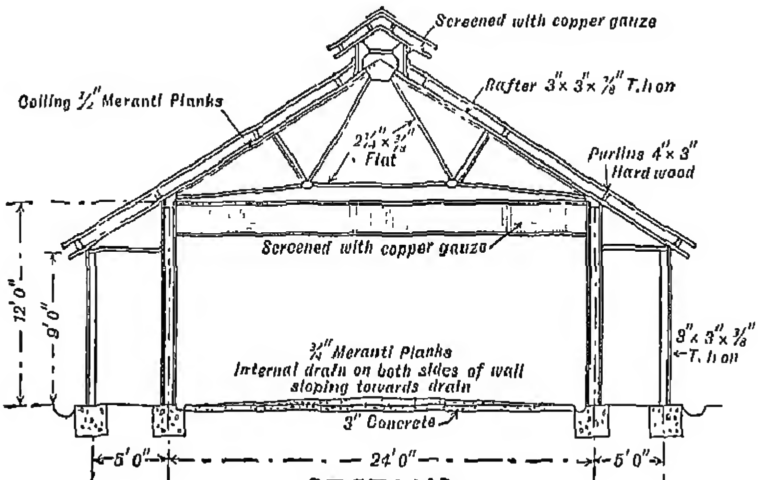
FIG. 72.—Plan of mosquito-proof house.
From S. P. JAMES's *Malaria at Home and Abroad.*

All must be screened. The effective adaptation of screen cloth to ventilators, as in all screening work, is mainly a matter of good carpentry.

Mosquito-proofing of verandahs.—This, if properly and completely done, is rather expensive, but is a great comfort. Its disadvantages are that it reduces the light, retains some of the heat, and interferes with the free movement of the air. For ordinary endemic malarious places the conversion of the whole or a portion of the verandah into a mosquito-proof room can be carried out with the most satisfactory results at comparatively small cost. Wire-gauze panels, the size of the openings between the columns or upright beams, can be

India, as early as 1828, recommended the use of mosquito nets as a preventive measure against ague. At that time they were used to exclude *miasmata*, which were supposed to give rise to the disease, or to prevent chills from the night dew. They were likewise used to avoid the nuisance caused by mosquitoes long before we knew that anophelines were malaria vectors.

The mosquito net.—The proper use of mosquito nets, without any other measure, is capable of preventing malaria in the most virulently infected districts. The net must be free from perforations, otherwise it becomes a mosquito trap. It must be so wide that no part of the sleeper's body is assailable by mosquitoes during the night. The net should be hung inside the poles, thoroughly tucked under the mattress (not hanging on the floor), and it should be stretched tight. A loose, sagging net checks the perflation of air through it, and becomes oppressively close. The length and width of the mosquito net should be the same as the dimensions of the bed; the height should be about $3\frac{1}{2}$ or 4 feet above the bed, and reach to 10 inches or so below the mattress or bedding. It is desirable that the angles of junction of the netting should be



SECTION

Fig. 73, II.—Screening of a hospital.

strengthened by strips of calico or tape. As the width of the ordinary bed is such that in moving the limbs about during sleep they come into contact with the net, it is necessary that the lower 12 inches of the net be covered with a double thickness of calico or *mulmul*. A greater depth of this thick material would interfere with the ventilation through the net and make the air within close and unpleasant. The net should be put into position at sunset, its interior examined before going to sleep, and any mosquitoes discovered killed. The mesh should not be too coarse, as mosquitoes, especially Anopheles, are expert in wriggling themselves through a large mesh; fourteen or sixteen strands to the inch is the right gauge (p. 305). Except when punkahs or electric or oil-driven fans are used over the bed, the top of the net should consist of calico or a double thickness of *mulmul* or muslin, and not mosquito netting; this prevents bird-droppings, insects and dust falling on the top. When the ordinary overhead punkah is in use, the frame supporting the net and the poles should not be more than $2\frac{1}{2}$ feet above the bed; in this case the top of the net should consist of ordinary mosquito netting.

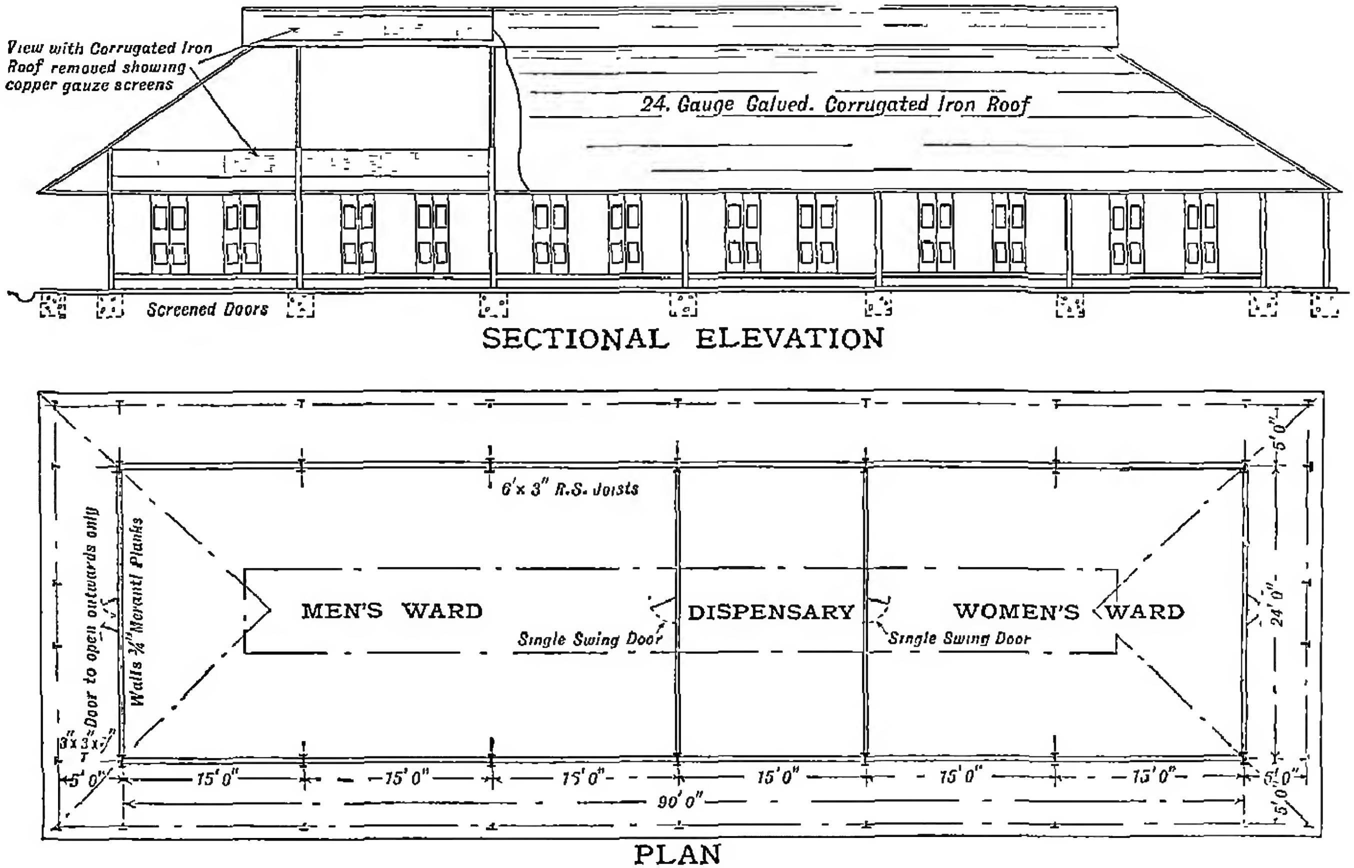


FIG. 73, 1.—Screening of a hospital

veil is the "Mosquinette" (see p. 62, and pp. 396, 397, Figs. 107, 108). It is made on the same principle.

Gloves may be used to protect the hands, but even when carried they are seldom worn on account of the heat.

Mosquito boots.—These are made with the upper part reaching well above the knee, the trousers being within the legging part of the boot. They are best made of canvas or stout drill (Fig. 74). Those of thin untanned leather are very warm. Thin soles only are required. The boots should have straps on the outer side of the upper end, so that they can be attached to the trouser buttons. The writer, after using several kinds of foot protection, finally came to the conclusion that two pairs of socks, or preferably a pair of socks inside and knickerbocker stockings outside them, are the most convenient. Women are best protected by canvas gaiters or putties or two pairs of stockings.

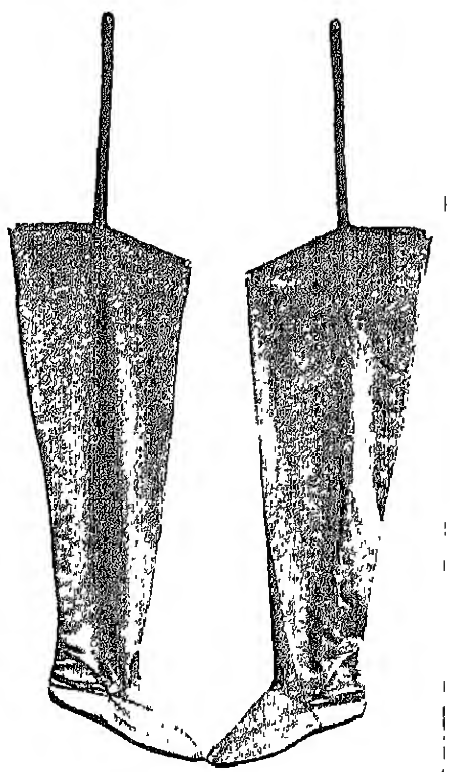


FIG. 74.[1]—Long mosquito boots Wellcome Bureau of Scientific Research.

Tinctorial prevention of mosquito bites.—The tinctorial prevention of mosquito bites is not without its importance; such colours as navy blue, dark red, reddish brown, and black are more attractive to mosquitoes than articles of white, slate-grey, green, light yellow, and violet, and it is probable that the white clothes worn by inhabitants of the tropics generally serve a useful purpose in this direction.

Reduction of hiding-places.—Hangings, pictures, clothes, etc., should be reduced to a minimum.

(iv) *Culicides* [2]

Various forms of culicides have been in use almost from time immemorial; but we need here only refer to those employed in modern times.

Adult mosquitoes may be destroyed by various *gases, fumes* and *odours*.

Direct destruction of adult mosquitoes by fumigation.—Fumigation with certain agents is the most immediate way of destroying mosquitoes present in houses and huts. The methods in use are connected with the vaporisation of chemical substances. Rooms to be fumigated should be measured, and the amount of material used based on the cubic space; guess-work means slackness and inefficiency. All precautions against fire should be taken. Fumigate for two to three hours. When fumigation is complete and the room ventilated, the floor

[1] Reproduced from Dr. ANDREW BALFOUR'S article, "Personal Hygiene in the Tropics," in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. I, p. 33.

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What is meant by the term MESH? The writer would make a brief digression here to borrow an explanation regarding the use of the word *mesh*. Colonel W. P. MacArthur[1] has cleared up all doubt as to what is meant by mesh in connexion with wire-gauze and mosquito netting. "It is impossible to measure cotton nets in the same way as wire gauze (screen cloth). In the latter, parallel wire strands cross one another at right angles, and it is easy to count the number of holes in the linear inch, though their size is affected by the diameter of the wire. Wire with a diameter of 0·0148 inch to 0·0068 inch is generally used, and it may be made in order of expense from steel (painted), galvanised iron or steel, brass, copper, oxidised copper, monel metal and 'Grenite,' the last two being specially valuable for hot, damp climates.

"To estimate correctly the mesh of cotton nets a count is made of the number of holes along a line of the warp (horizontal) and that of the bobbin or woof (diagonal) falling within a supposed square inch; the hole at the angle of the squares is counted twice. The two main counts are added, and this gives the figure for the mesh. The line of the woof is more loosely woven than that of the warp; cotton is graded according to weight. Washing or exposure tends to make the count of the cotton net go up one. A 14-mesh 'screen-cloth,' contrary to prevailing ideas on the subject, seems to be quite effective in excluding *Stegomyia fasciata*." [2]

One great advantage of screen cloth is that, if it is too fine, no harm is done; it is a fixture for the time being, whereas unnecessarily fine mosquito netting is discarded. Where mosquito nets are in use in the Army, especially in the hot, steamy weather of the rainy season, troops often put them out of action at night.

(ii) *Use of Punkahs and Electric Fans*

Punkahs and electric and lamp-driven fans are useful in keeping off mosquitoes on the plains, and advantage should be taken of their use by all persons able to afford them during the anopheline season. The electric fan has in many stations in India added considerably to the comfort and health of Europeans. Mosquitoes dislike the agitation of air set up by electric fans and punkahs. Electrically propelled punkahs with adjustable fringes are now extensively used in British barracks. They fill a great want. They are cool, and if intelligently used, effective. The fringe should be at least 5 feet long, and be capable of being lowered to a foot from the man's face. The height of the fringe is regulated by means of a thin rope, and as the adjustment has to be done while the fan is in action, the men sometimes swing their whole weight on the rope, which, of course, breaks. Hence constant supervision and repairs are required to keep them efficient. A lamp-driven fan is effective and portable, and eliminates the punkah coolie.

(iii) *Mosquito-Proof Clothes*

Anti-mosquito veils.—In very malarious places persons moving about in the evening and at night should have their head, arms, feet and legs properly protected from mosquitoes. Men on sentry duty at night frequently acquire malarial infection. Anti-mosquito veils for the face are worn by railway officials in certain districts of Italy. They were likewise distributed in the Japanese Army, in 1904 and 1905, during the Russo-Japanese War, and consisted of a cylinder of mosquito netting closed at the top, supported by a collapsible framework, all held in position by tapes. A good type of veil is the "Simpsonette," devised by Lady (W. J.) Simpson. Another useful

[1] "Mosquito Netting," *Jl. Roy. Army Med. Corps*, January, 1923, pp. 1–11. This paper should be consulted for valuable details and for the table regarding screen cloths.

[2] From *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XVI, No. 7, January 18, 1923.

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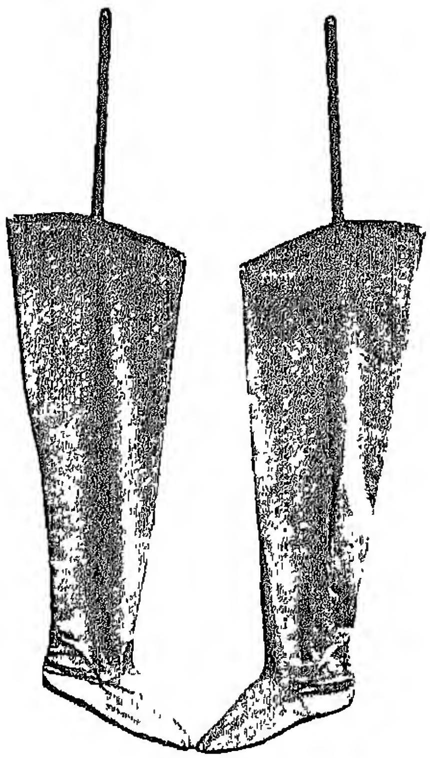

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and walls should be swept and the sweepings burnt, because some of the mosquitoes may only be stupefied. Never rely on the general statement that a house has been fumigated. This often means that a few ounces of sulphur or other substance have been burnt in each room. If there is a sanitary inspector or mosquito inspector, this work should be carried out by him.

Sulphur dioxide.—Sulphur dioxide is one of the best direct general fumigant culicides. There are several kinds of sulphur (*gundak*) in Indian bazaars, and some of them are reputed to contain a small amount of arsenic. All varieties purchasable, however, may be used for fumigation.

Sulphur dioxide may be used :—by burning crude sulphur in an iron vessel standing in water, by means of tubes of liquid SO_2 (under pressure), by generating it in special apparatus outside the room, and in other ways. It is essential that 3 per cent. of the gas be obtained as a minimum This means death to all insects. The action of the gas is intensified by heat and moisture The third method referred to, when the generator and compartment are in one circuit, ensures control and penetration.

When solid sulphur is used the strength required is 2 pounds per 1,000 cubic feet of air space. The addition of a little kerosene or methylated spirit accelerates the action It is useless to attempt this method of fumigation by burning a little sulphur in one place and closing the doors and windows. For the gas to be effective the sulphur should be placed on a fairly large protected fire. Weak doses of the fumes only stupefy the mosquitoes ; they fall to rise again.

When cylinders of compressed SO_2 are available a sufficient number of 20-ounce cylinders to produce 6 pounds of SO_2 to the 1,000 cubic feet are required. Distribute a number of *baltis* (pails) containing damp cloths in the room. The gas is set free by cutting off the vent pipes ; the cylinders are then placed nose downwards in the *baltis*. An operator, if not very expert at the job, is seldom able to tolerate more than the effects of four tubes, so that, unless the room is very small, effective fumigation for insecticidal purposes is not completed ; a relay of operators may be necessary.

One of the most useful of all fumigators for houses is a small-pattern portable Clayton apparatus for diffusing SO_2 gas, but for barrack rooms, hospital wards and large chambers generally the most effective method of fumigation is that with the large Clayton apparatus, in which the strength of the gas formed is under control from the start. Mosquitoes in steamers can be destroyed by the Clayton SO_2 apparatus or a smoke machine. The latter may be also used in trains.

Fumigation with formaldehyde.—Formaldehyde gas is a powerful insecticide when in sufficient concentration. It is easily diffused by vaporising paraform tablets in an "Alformant" lamp. For efficient use thirty tablets are required per 1,000 cubic feet, and one lamp per 100 square feet of floor space. The tablets are placed in the upper part of the lamp and the spirit stove beneath lighted. An exposure of several hours is necessary, and thorough ventilation of the room is required afterwards. The British Red Cross Mission used this method during the anti-malarial campaign among the Greek refugees in Western Thrace and Macedonia in 1923. There are several other patents of the kind on the market, all more or less efficient. Formalin gas is also readily generated by pouring 10 ounces of formalin on 5 ounces of potassium permanganate ; this quantity is required for 1,000 cubic feet of air space. The generation should be carried out in an iron vessel. On the whole the writer doubts whether formaldehyde fumigation is better than that of SO_2 when the latter is properly used.

Camphor and carbolic acid or cresol.—The former combination is largely used in the United States, especially on the seaboard in regions of endemic yellow fever, for the destruction of *Stegomyia callopus*. Equal parts of crystallised carbolic acid and camphor are dissolved by gentle heat, 4 ounces of each per 1,000 cubic feet being put into a small pan suspended over a spirit or petroleum lamp and left for two hours. A white vapour having an agreeable

smell is given off. The fumes do not injure anything in the room, and the latter can be occupied immediately after use. The writer has used this extensively, and knows of no better fumigant. Cresol may be used instead of carbolic acid. Cresol or carbolic acid alone is effectual, but a much larger quantity is required. Camphor alone is useless.

Culicides are unreliable in a large campaign against mosquitoes. They are useful in single houses, in barracks, hospitals, hotels, etc., exactly, that is, where screens are applicable.

Chlorine-gas fumigation is also efficient and speedy in destroying mosquitoes and is easy to carry out in the orthodox way.

Fumigation with culicidal fumes as a general anti-mosquito measure is most useful at the end of the breeding season of mosquitoes, about the middle of spring and again before the rains set in. These are the times when hibernating and æstivating anophelines may be destroyed and prevented from giving rise to vast broods during the ensuing breeding season.

Country tobacco smoke.—To rid of mosquitoes a room of 3,000 cubic feet capacity saturate 1 pound of country tobacco leaf (which can be purchased in every bazaar) with kerosene oil in the bottom of a kerosene oil tin and set it on fire—no mosquito survives.

Powdered pellitory root pastilles.—Pastilles of pellitory root burned in rooms reduce the number of adult mosquitoes. The smoke of the burnt powdered root rapidly stupefies them; they fall to the ground and may be collected (on old newspapers or white sheets spread on the floor), and destroyed, or they may be swept up and cremated. About 2 tablespoonfuls made into a cone and burnt from the top is enough for a room of 4,000 feet capacity.

"There is a custom among Indian people of hanging small bags containing garlic and camphor round the necks of sick patients, especially children, with the idea that evil spirits may be warded off. This really keeps off mosquitoes." [1]

Smoke.—To drive mosquitoes out of a house any fuel burning with a dense smoke will suffice. The *doors* and *windows* must be *left open* during the process, and closed at once when they have made their exit. After they are driven out they must, if possible, be prevented from returning. Or the mosquitoes may be captured and killed by covering all openings except one with dark material, the exception being covered with a white sheet. To this the stupefied mosquitoes will swarm, and may be killed. The procedure is best carried out about evening or in the early morning; it is simple, primitive, costs nothing, and gives a fair idea of the numerical prevalence of the various kinds of mosquitoes. It is a good way of getting rid of hibernating mosquitoes in the poorer quarters of towns and villages. It is not, however, suitable for thatch houses or houses with low wooden roofs.

Spraying with culicides.—In some special circumstances, as in the case of lofty roofs and high walls, spraying with culicides is recommended; one of the best is formalin solution. There are several forms of spraying apparatus on the market; a very effective one is Mackenzie's Spray. The solutions are applied from below upwards, the spraying being done from side to side; this secures equal distribution.

Spraying with formalin solution.—In working with *formalin solutions* the operator should wear a veil to escape irritation of the eyes by the fine spray. About 1½ gallons (1 per cent.) of the solution are required for each 1,000 square feet of surface; it takes an hour to do the work; all apertures should be sealed by means of stout paper and flour or *atta* paste. Unused chimneys are favourite resting-places for mosquitoes, hence the upper opening and not the lower is sealed.

The Giemsa spray.—This is a useful agent for destroying mosquitoes in rooms. It

[1] B. N. Ghosh and J. L. Das, *Treatise on Hygiene and Public Health*, 3rd Ed.

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Among OTHER REPELLANTS recommended by various authorities are: Crude naphthalene 4 parts, camphor 1 part; kerosene scented with 6 per cent. of oil of bergamot; oil of eucalyptus with 1 per cent. of carbolic acid; "Parasitox" (a proprietary preparation, safrol being the main component); spirit of camphor; oil of pennyroyal; essence of peppermint; lemon juice; vinegar. The bases of practically all the better proprietary culicides and culicifuges are—citronella, eugenol, carbolic acid, safrol, cinnamic aldehyde, naphthalene, camphor and kerosene; soap, vaseline and vegetable oils are used as vehicles and evaporation retarders

Most repellants evaporate within a few hours and the mosquitoes return, but they afford a certain amount of protection from infection and add to comfort when mosquitoes are numerous.

(c) OTHER MEASURES

Mosquito baits.—It is possible that we shall find one or more scents that attract mosquitoes. This would be a great discovery, for if such a scent, or any agent attractive to mosquitoes, were found, many of the exceedingly difficult problems that beset the anti-malarial sanitarian and municipal administrator could then be solved. HANSCHELL has recently pointed out that a mosquito trap may be baited by a negro's sweat-soaked vest.[1]

Hand nets for catching mosquitoes.—The destruction of mosquitoes by hand is not to be ignored, and in isolated houses, barracks, hospitals, out-offices, etc., a considerable number of infected mosquitoes may thus be got rid of. The most effective way of catching them is by means of a hand net made like a small butterfly net. In the military cantonments in Burma barrack rooms were provided with hand nets; they were very successful.

Capture of mosquitoes in test tubes.—In the unscreened British barracks of Maymyo (Burma, 3,900 feet high) twelve soldiers captured in test tubes during the mosquito season an average of 28·33 mosquitoes in an hour, the total captures in six rooms being 170. In a similar series of observations in Mandalay the average captures per room were 31, and at Bhamo 29. Even this method is not altogether negligible.

In some places where intensive anti-malarial campaigns were being carried out the whole population was induced to help in the destruction of adult mosquitoes; a small reward was given for captured anophelines. In one locality catch cups made of bamboo were distributed for the purpose.

Fly swat for destroying adult mosquitoes.—The ordinary fly swat or *makki-mar* is very useful for killing mosquitoes when they are resting on walls, clothes, etc. One of the best kinds is a small square (6 in. × 8 in.) of flexible wire gauze bound at the edges and set in a wooden handle. "Swat the fly" is a well-known auxiliary for killing flies; it is an equally valuable accessory in reducing adult mosquitoes in barracks, hospitals and houses. Daily systematic swatting, catching and killing mosquitoes was a potent means of lessening these insects in the Panama Canal Zone. These last three measures are most useful in barracks.

"*Tangle-foot*" *as a mosquito trap.*—Sheets of glass, celluloid or talc covered on both sides with a mixture of equal parts of resin and country castor-oil heated together ("tangle-foot") and set a few feet apart at right angles to one another will indicate the direction from which mosquitoes come and point to their breeding-places. If the plates are acting well, the number trapped may give some idea of the prevalence of these insects, and its variation from day to day. Some dark, quiet, daytime resting-place for mosquitoes might be created and covered with "tangle-foot," or the latter may be spread on one side of large sheets of thick paper, and adjusted to the angles of the walls in the dark corners of rooms.

[1] *Trans Roy. Soc. Trop. Med and Hyg.*, Vol. XX, No. 3.

consists of—tincture of pyrethrum 480 grammes, odourless potash soap 180 grammes, glycerine 240 grammes. Before using, dilute with twenty times its own weight of water. Spray the walls of a room with a spray lamp. The tincture is made by macerating 20 parts of pyrethrum blossoms in 100 parts of alcohol.

Creosote spray.—Of two parallel bridges (one the ordinary highway, the other the railway; one constructed of wood soaked in creosote, the other of untreated timber) there were beneath the first very few mosquitoes, beneath the other always thousands [1] Creosote sprinkled about rooms effectually gets rid of mosquitoes. It is, however, doubtful whether many people would care to breathe for any length of time an atmosphere permeated with the vapour of creosote.

It is possible we may one day be spraying, distempering or washing walls with some kind of permanent insecticide that will prove too repulsive for mosquitoes.

(v) *Culicifuges*[2] *and Mosquito Repellants*

Essential oils.—Various chemical and mechanico-chemical agents have been used to apply to the skin of the face, neck, hands and other exposed parts to keep off mosquitoes. They are usually odorous substances in the form of culicifugal ointments, oil of eucalyptus, oil of rosemary, oil of lavender, oil of anise, oil of lemon grass and essential oils generally, kerosene oil and various washes.

The application of the *essential* oils wards off mosquitoes to some extent—one in great favour in India is *citronella* or *lemon-grass oil,* which is harmless and procurable from chemists in India, and in many large bazaars. It is one of the most agreeable and efficacious of the repellants now in use. It is the oil distilled from several species of Andropogon. The specimens of lemon-grass oil met with in India differ somewhat in appearance. The true oil is of a pale, shiny colour, transparent, with an extremely pungent taste and a peculiar, fragrant, lemon-like odour. In bazaars it is known as *akya ghas ka atr.*

Bamber oil.—In the Great War the Army on the Frontier in India and in Mesopotamia used this preparation extensively. It consists of citronella $1\frac{1}{2}$ parts, kerosene 1 part, cocoanut oil 2 parts, carbolic acid 1 part; the last-named is a preservative. The application remains effective on the skin for a few hours; it is most conveniently used from a scent sprayer or drop bottle. The essential oils are also best applied in this way.

"L.S.T.M. Repellant"[3] is an excellent substitute for Bamber oil: oil of cinnamon 2 drachms, oil of cajuput 1 drachm; formalin (40 per cent. formaldehyde) 1 drachm, alcohol (90 per cent.) $3\frac{1}{2}$ ounces.

Spraying the walls, roof and floor with mosquito repellants.—One of the most useful of these is the kerosene used for oiling collections of water, or ordinary kerosene oil. It is specially indicated for the mud walls and floors of huts. This use of kerosene is but little known and thus seldom practised. Sprayed or sprinkled two or three times a week, it tends to keep mosquitoes away. The odour is not over-pleasant, but it is some compensation that it is greatly disliked by the mosquito. The use of repellants, however, is no real safeguard against the attacks of mosquitoes, for they can enter houses, feed, and then, if they dislike the repellant on the wall, roof or floor, leave the house and find refuge elsewhere.

The writer has often coated his legs with kerosene and left them bare under the table in the evening, and on one occasion watched seven anophelines and two culicines gorging themselves with blood. The sprinkling of kerosene oil about the bedroom and tying a towel soaked in the oil to the bed-posts above the head are very inefficient, but not altogether useless, substitutes for a mosquito net.

[1] C. P. Coogle, "A Preliminary Report on the Use of Creosote Oil as a Mosquito Repellant," *U.S Public Health Rep.*, 1923, Vol. 38, No 1, pp. 437, 443.

[2] *Culicifuges* are agents that prevent the bites of mosquitoes.

[3] The initial letters of London School of Tropical Medicine. From Manson's *Tropical Diseases*, 8th Ed., p. 91

outhouses, adjacent culverts should be oiled from time to time. Thick, heavy foliage should be thinned, and, if necessary, sprayed with oil. The lawn hose should be used no more than is absolutely necessary, and never sufficiently to create dampness about the house. The effects of these few measures are at first surprising; they disperse the colonies of mosquitoes that have been in local residence for some time. New broods, however, will invade the area and find sanctuary until they likewise are dispersed. The writer for years adopted these harassing tactics, as supplementary to other anti-mosquito operations, always with temporary success; they cannot be relied upon alone.

Animal screens—diversion of mosquitoes from man to animals.—Some years ago it was observed that in some places mosquitoes were more numerous in cow-byres and stables than in adjacent human dwellings. It was further ascertained that some animals were more attractive to mosquitoes than man, and it was considered that the cow was one of these. The building of cowsheds near human habitations was found, in several places, to divert mosquitoes from man to the cattle. The idea was put forward by RIZZI and forgotten until ROUBAUD independently re-introduced it.

ROUBAUD believes that the stable or cow-byre most attractive to *Anopheles maculipennis* must not be over 3·5 metres in height; it should be sheltered from wind and sun, and animals must be regularly stabled therein, the intention being that the mosquitoes, having found happy conditions for food and housing within a few feet of one another, will rest therewith content. In such a stable or byre many mosquitoes hang replete, the neighbouring human dwelling-houses being empty of them. Such animal houses, properly placed, built and used, can, it is believed, be made effective screens to keep human beings free from anopheline attack.[1] (See Appendix VI—10.)

There are in British India 146 millions of bovine cattle, and many millions of horses, ponies, donkeys, camels and goats. If in suitable conditions they effect the diversion under reference, everything feasible should be done to bring those conditions into existence. It may be that this vast number of animals has had something to do with keeping malaria within bounds in India. The use of animals as a living defence between mosquito breeding-grounds and human habitations has gained in favour in the last few years. It is claimed by some authorities that the unintentional application of some of the conditions laid down by ROUBAUD is responsible for the gradual elimination of malaria from Denmark. In the Dutch East Indies there has been a belief that a screen of cattle has considerable value in preventing malarial infection in human beings. The latest investigations show, however, that the optimum anopheline host there, *A. listoni*, is not attracted to cattle.

The writer is not satisfied that the effect of animal screens in diverting mosquitoes from man has been sufficiently worked out at present to base any expensive measures on it; more observation, experiment and detailed investigation are required. So far it would seem that it is mainly a question of the food preferred by the Anopheles, and to a less extent of the relative numbers of human beings and animals.

B.—DESTRUCTION OF MOSQUITO LARVÆ BY LARVICIDES, ETC.

Larvicides.[2]—During the aquatic stages of the existence of mosquitoes their powers of resistance differ—the eggs are moderately, the young larvæ

[1] ROUBAUD and M. LEGER, "Observations sur la Paludisme en Corse," *Bull. Soc. Path. Exot.* (mars-avril, 1921); *Trop. Dis. Bull.*, Vol. 18, No. 5, p. 320.

[2] "Larvicide" is here used to imply an agent which destroys the larvæ of mosquitoes.

Clearing and burning of jungle and scrub.—Adult mosquitoes dislike sun and wind, and anophelines are weak fliers. Many mosquitoes take shelter and are hidden in long grass, scrub and brushwood, and creepers near inhabited dwellings. The proper time for jungle cutting is either at the beginning of the hot weather or after complete cessation of the rains. The vegetation should be cut down, and after being allowed to dry should be burnt on the ground, which should be dug over so as to tear up and destroy the roots. The use of *flame throwers* will greatly economise labour when the area to be dealt with is extensive. Annuals should be destroyed before the formation of the seeds. Before the work is started all doors and windows, and other means of ingress for mosquitoes to adjacent buildings, should be closed, as the insects will fly to them when driven out of cover. This is one of the simplest, easiest and least costly ways of reducing mosquitoes, but it has to be carried out periodically unless the area concerned can be properly beaten down, paved, concreted, asphalted or turfed. Hidden breeding-places concealed by vegetation, land springs, small artificial water containers, and even wells are sometimes met with in adopting this measure. It is a mistake, however, to cut down and burn jungle indiscriminately in the belief that it harbours mosquitoes; doing so may give Anopheles an avenue from infected buildings or huts, or from breeding-places. The problem in each instance should be carefully studied before any action is taken.

To drive mosquitoes from rooms mechanically.—Open all doors, windows, cupboards, and shake all bed-hangings, clothes, boots, etc. Then with a long broom sweep the ceiling, walls, top, back and interior of wardrobes, bookcases, cupboards and all dark corners. Dust the back of pictures, top of curtain poles, and under-surface of all chairs. Close the doors and windows when the chase is over. The application of the blow-tube or the exhaust pipe of a vacuum cleaner will be found most useful where electric fans or lighting is installed. These tubes and pipes can be used over any kind of surface—walls, roof, top of cupboards, etc.

The effects of vegetation.—Some plants, such as the castor-oil bean plant, are reputed to keep mosquitoes away from houses, but so far none have proved useful in this direction.

Pineapple and **banana** plants foster mosquitoes. They should not be cultivated in the immediate neighbourhood of human dwellings.

Cocoanut, date and areca palms as breeding-places of mosquitoes. Reference has been made to the discovery in the Tanga district of East Africa that mosquitoes breed in cocoanut palms (p. 130). It is highly probable that they breed also in date palms and areca-nut palms. The writer understands that date palms in Egypt have been connected with "fever" for centuries. So far it has not been found feasible to use larvicidal substances regularly for the crowns of the palms; the difficulties are too great. If palms are proved to be breeding-places of malaria-carrying Anopheles in India, the further planting of them within towns and villages should be stopped, those now in existence should be gradually eradicated, and the people informed as to the danger of building near palm groves.

Harassing adult mosquitoes to effect their reduction.—The favourite mosquito haunts in the neighbourhood of the average human dwelling are bushes, clumps of weed, high grass, cellars, underground dwellings generally, under culverts and bridges, stables, outhouses, dark, sheltered parts of ruins, in each of which there is a certain amount of moisture and absence of direct sunlight. The jungle, weed, scrub, high grass within 200 yards of dwellings can be cut down and burnt. The ground under the house, the cellar, stables,

days, and reaching the pupal stage in a week. Hence, when the temperature is exceptionally high, and then only, oiling may have to be done twice a week. *Per contra*, in cool weather the development of the new brood is correspondingly delayed.

There are various kinds of mineral oil. The heavier ones are more destructive to mosquito larvæ than is kerosene. What is wanted is a mixture of one of the heavy oils with kerosene that will spread immediately over the surface as a fine film. If there are any visible globules the mixture requires thinning down with more kerosene. It will usually be a matter of experiment as to what quantity of kerosene is necessary to make a mixture that will spread immediately and uniformly and not clog the sprayer. Speaking generally, the best mixture is heavy oil 66 parts, kerosene 33·5 parts, and indigenous castor oil[1] 0·5 part. Proper mixing requires vigorous stirring until the mixture has merged into a quick-spreading fluid. Castor oil greatly increases the spreading power, uniformity, tenacity and cheapness of the film.[2]

Much oil is wasted in an attempt to obtain a thick film. Where the water is clean a film just thick enough to give a play of colours is sufficient. Where the water is foul or covered with a scum more oil is needed; experience teaches exactly how much is required in different conditions. The oil should be thin enough to cover the whole area. When there are breaks in the film, larvæ may sometimes be seen proceeding towards them.

The writer has repeatedly "dipped" successfully for anopheline larvæ in places that had recently been improperly oiled.

Oiling versus drainage.—If properly carried out once a week during the breeding season, oiling destroys every Anopheles larva and nymph in the area concerned, besides many of the adult females that rest on it to lay eggs; and it prevents further laying of eggs while the film retains its strength. It is, therefore, a speedy way of establishing Anopheles control over limited areas. Oiling can be commenced at once everywhere; there is no reason for inactivity. There is no large initial outlay—a point of some importance to poor communities. But the expenditure on oiling, including the wages of mosquito gangs and their supervision, is continuous from year to year. On the other hand, drainage usually involves a heavy initial expenditure, but, once carried out, it requires less responsible supervision; collections of water over the drained area are visible at once if any defects exist.

Oiling is of easy application to the vast number of small rain-water pools, too numerous to drain and too evanescent to stock with fish, though often of sufficient duration for one brood of Anopheles. This is its use *par excellence*, and so far as can be seen, this use will continue until something better has been discovered. Oiling is also a most valuable means of tiding over the period during which permanent methods of controlling Anopheles are being brought into operation. Thus, for example, the edges of tanks, ponds and streams may be oiled while larvæ-concealing vegetation is being removed to facilitate control by means of fish, and while drainage schemes are being carried out oiling has to be continued. The oiling must be practised, not only within any selected area, but sufficiently far afield to be effective against Anopheles visiting it. Neglect of this is one cause of so-called failure of oiling. Personally the writer considers a quarter of a mile outside inhabited dwellings quite sufficient.

[1] Indigenous castor oil, obtainable in every bazaar, mixes up to 2 per cent in the hot weather with mineral oils without separating out; even 0·1 per cent greatly improves the usefulness of the mineral oil, and the higher the concentration up to 1·5 per cent. the better the mixture.

[2] W. NORMAN LEAK, *Jl. Trop. Med. and Hyg.*, 1924, pp. 37–40

feebly, the adult larvæ and nymphæ very resistant. The nymphal period is, however, comparatively evanescent.

True larvicides are often poisonous to man and beast, and on the whole are less effective and more expensive than oiling. They usually mix with water and poison it, killing the larvæ rapidly in most cases. The great advantage of true larvicides is that they are more thorough and lasting in their effects, and are not affected by weather conditions, as are oil films. They cannot be used in India for reasons stated later on. Where the oil film is washed away by heavy rain or blown aside by strong wind a larvicide is indicated.

Larvicides can only be effectually and economically used when a preliminary survey has been carried out, and all breeding-places have been marked on a skeleton map. Only those known to contain Anopheles larvæ should be treated, and if the survey has been really complete, only those containing malaria-carriers should be marked on the map for treatment.

The chief agents employed as larvicides are petroleum in various forms, aniline dyes, and certain mineral and vegetable products.

Petrolege.[1]—The process of *petrolege* was commenced in the United States of America by O. Howard in the year 1892. It is probably the most extensively employed anti-mosquito measure in India at the present day. The total amount of money spent on petroleum for this purpose is considerable.

In the early days of the use of kerosene for oiling the places in which mosquitoes breed, it was considered that this process destroyed the larva by forming a film on the surface impenetrable to air, and at the same time plugged up the breathing openings with oil, in short suffocated it. The oil was also thought to reduce the surface tension so that the larva could no longer support itself in the water. It has since been suggested that oil acts as a poison through solution in the water, or possibly that it penetrates and blocks up the smaller branches of the tracheæ and poisons the tissues directly. By coloration with aniline dyes it has been shown that contact of the siphon with the oil leads to immediate blocking of the respiratory apparatus, the oil entering by capillary attraction, and the larva dying by suffocation within thirty to sixty minutes. It is difficult to separate the suffocative action from the toxic; immersion in the oil kills in five minutes. The rapidity of death depends upon the toxicity and volatility of the oil used.

It is possible that the oil has the indirect action of altering the quality of the water in some way that makes it unfavourable to mosquitoes. Sir Malcolm Watson has observed that at the bottom of certain pools in ravine streams there is a "felted alga"; these pools are not used by *A. maculatus* for oviposition. The felting differs from the loose, floating tangle of the ordinary alga. It was observed that wherever a ravine was thoroughly oiled the ordinary alga died; in its place the felted alga appeared at the bottom. This is a subject that calls for investigation. (See Appendix VI—11)

Anopheles larvæ succumb to oiling more readily than Culex larvæ. A good film covering a pond or pool will kill all the Anopheles larvæ in an hour or so. Culex in the same circumstance may survive for one, or even two, days. After one brood is killed off, several days must elapse before another can develop. Close observation has enabled the writer to ascertain that while the film remains Anopheles will not lay eggs, or, if they try to do so, succumb in the effort. In very hot weather, however, the film disappears within a week; Anopheles may once more oviposit in the water, a second brood appearing in three or four

[1] *Petrolege* is the application of petroleum or some of its products to surface collections of water to destroy mosquito larvæ.

matic dropper containing the petroleum mixture may be suspended over the canal.

Wheeled may be preferable to man-carried sprayers. Accordingly various kinds of pumps are adapted to barrels and small tanks; the barrel can be mounted on a cart frame (Fig. 76), or on a truck, waggon or boat. In some of these pumps the pressure can distribute the stream of oil 50 feet or more. They are of no use in swamp work or in rough timbered areas, and they lack the great advantage of the knapsack—portability. They are very useful for long lines of borrow-pits at the sides of roads, along railway lines and for oiling parts of lakes, tanks and ponds, the edges of rivers and streams and pools in the open. In the Panama Canal Zone they use punts with engine-driven sprayers aboard.

The organisation.—In all large towns and cantonments where oiling has to be carried out on a large scale it is essential to organise a method by which the oil will be stored, distributed and transported. For men to carry a few bottles of kerosene oil and, under the direction of an overseer, to pour a little over any water surface pointed out is a futile waste of public funds.

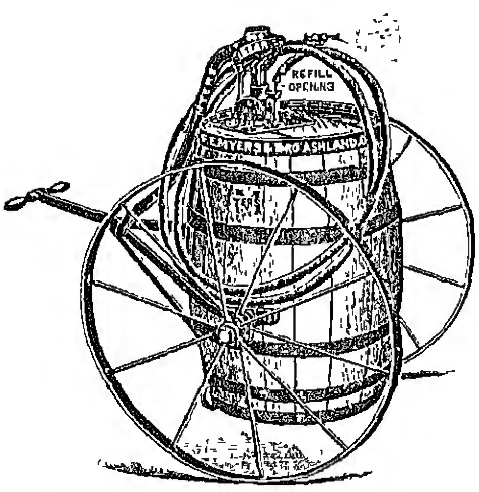


Fig. 76.—Barrel sprayer mounted on a cart frame.

In an ordinary inland town of 25,000 inhabitants oiling operations will be scattered over a few square miles, and since every spot which requires oiling should be treated once a week, the supply of oil required for the season is considerable, and should be assured and stored at some central depot adequately protected against fire, and ready mixed for use. Arrangements for daily distribution are equally essential, either direct from the central depot or from conveniently placed sub-depots. One or more drums or barrels, provided with taps and mounted on wheeled frames either man-hauled or drawn by pony or bullock, and driven preferably by the overseer, accompany each gang. The overseer takes his gang to each selected spot, sees that the men's containers are kept supplied, and that all places requiring it are properly oiled. The area for which he is responsible will have been divided into six portions, on one of which work will be undertaken each week-day. He is responsible that the supply of oil is sufficient and is locally available, without having to send for it. If oil can with certainty be requisitioned locally, arrangements for storage are unnecessary.

Drip-cans or barrels can be employed for the continuous or intermittent oiling of flowing streams. They consist of oil containers so arranged that a small quantity of the fluid drips from a height of 3 or 4 feet (or higher if the oil is heavy) upon the surface of the water. The drops being broken by impact with the water, the formation of a proper film is accelerated, covering pools and backwaters provided vegetation and obstructions are absent (Figs. 77, 78 and 84).

In the malarious cantonments of Burma in 1912–13 the writer used drip-

In determining whether oiling is required, we should consider the temperature, topography, aquatic vegetation present, presence of larva-eating fish, nature of the breeding-places and other points.

A few winter oilings for anopheline vectors which hibernate in the larval stage would be very valuable.

In connexion with large tanks the writer's experience is that applications of petroleum are useless.

Sprayers.—For general purposes oil is best used from a sprayer. This is usually of the knapsack type. There are several knapsack sprayers on the market—Meyer's "Four Oaks," "Vermorel" and others. Meyer's knapsack sprayer (Fig. 75) is the most popular and best; it is used in the Panama Canal Zone. It consists essentially of an oil container, a pump, and a spraying nozzle at the end of a short rubber tube. It has metal valves, which are better than rubber or leather, holds 5 gallons of oil, and fits on the back like a knapsack, the pump

FIG. 75.—The knapsack sprayer.

being worked over one shoulder, a less arduous method than the side action of some sprayers, the spray tube being directed by the opposite hand. It will distribute oil satisfactorily to a distance of 20–30 feet, a noteworthy asset in swamp and scrub; the opening of the nozzle can be adjusted to deliver heavier oils than those ordinarily employed; the lever may be turned to either side and used in either hand; the weight is uniformly distributed, although with the can full it is fatiguing in the sun; finally, having both hands free is a great advantage when working over rough ground or in jungle. Men who use the sprayer for days on end are liable to suffer from a sore back, due to leakage of oil, an accident which can usually be prevented by avoiding filling the can too full, and by replacing damaged washers with good ones.

When the water surface is large, and its depth sufficient, spraying may be carried out from a boat. Canal beds in which the water is shut off periodically are a source of myriads of anophelines in vast tracts in India. In this case the oiling should be done with each flow of water through the channel, or an auto-

useful where there is much vegetation in the water and in low-lying marsh ponds. In 1909 the writer observed that the parts of tanks, ponds and *ghats* used by *dhobies* (who generally use lime soap for washing clothes) were free from mosquito larvæ of any kind, and he advised the employment of soap emulsion to prevent oviposition.[1] Its use has been advocated by Dr. ANDREW BALFOUR for Mauritius, and by other malariologists.

Paris green as a larvicide.—Paris green has been extensively used as a larvicide in late years, especially in the U.S.A. and France. When mixed with 100 parts of dust the water in which it is sprinkled is said to be harmless to man and animals. It is strongly recommended by many authorities. The writer has had no experience of its use in India.

Cresol.—In very dilute solution cresol is a powerful larvicide. One ounce of cresol in 10,000 cubic feet of water (1 in 10,000,000) kills larvæ in twelve hours; in 1,000 in four hours.

Infusion of tobacco leaf, the powdered unexpanded flowers of chrysanthemum, pellitory, fish poisons (especially *Derris* spp.), crude carbolic acid, lysol, permanganate of potassium and many other agents have been used as larvicides. None of them appears to be superior to an emulsion of heavy mineral oil 95 to 98 parts, kerosene oil 5 to 2 parts (according to the brand of heavy oil) and 0·5 part of indigenous castor oil, and the writer believes that it would be highly dangerous in India to use them.

The winter is a good time for destroying larvæ, as is also the beginning of spring, when they are fewer in number in the water and new generations are not being developed. For hibernating larvæ two applications of oil, one at the beginning and the other near the end of the cold season, are sufficient. In the winter, wherever adult mosquitoes are found they also should be killed.

As our knowledge of the habits of mosquitoes, of the localities in which and the time during which they lay eggs, increases, we will be better able to formulate methods to effect their destruction, but, even in the most favourable circumstances, the getting rid of anopheline larvæ will always be an arduous task when carried out on a large scale

A reliable larvicide still a desideratum.—It may be said that no really thoroughly reliable cheap larvicide, that can be universally employed in India, has as yet been discovered; and it will be extremely difficult to find one, as the people are in the habit of drinking and watering their domestic animals at almost any source of supply. The larvicide for general use in India should be completely and uniformly toxic to mosquito larvæ, reasonably lasting in its effects, usable in small quantities, speedy in action, able to mix rapidly with all kinds of water (including saline and alkaline), stable in constitution, non-toxic to man and domestic animals, harmless to plants, and inexpensive. The majority of larvicides in use have only a few of these properties. In Europe some of the aniline dyes had a vogue for a time, and were considered to be the most suitable and least expensive of the larvicides in use. The dyes used are poisonous to many aquatic larvæ and non-injurious to plants. "Larvicide" is the trade name of one of the most popular of them.

Prevention of mosquito-breeding in wells.—This is of much importance in India, especially in cities and towns. We have seen that *A. stephensi* breeds extensively in wells in Bombay and Madras, and in wells and cisterns in Calcutta. But the matter is associated with the difficulty that most of these wells are in private houses. The subject of sterilising wells against mosquito infection is still in the experimental stage. All the methods so far devised are too costly

[1] *Report of Malaria Survey of the 7th (Meerut) Division*, App. II, 1909

for general use. The writer considers that much further investigation is called for before it can be introduced as a practical anti-mosquito measure.

Various devices have been employed for killing imagines, such as floating evaporators, parachutes containing the apparatus for evolving larvicidal gases and shutting off the surface of the water from the body of the well, and other apparatus for generating culicidal vapours or gases near the mouth of the closed well. The methods used against larvæ may, in general terms, be said to consist in "gassing" the surface of the water with larvicides. So far the experiments have shown that—*formaldehyde*, evolved from a floated formalin lamp, kills half the larvæ in thirty-two minutes; *chlorine vapour*, generated at water level from bleaching powder and hydrochloric acid, kills larvæ in half an hour; SO_2 vapour, evolved into the air above the water, the sulphur being burnt in a brazier and the well kept closed for three to four hours, did not yield satisfactory results. Its effects are said to be due to the increase of the hydrogen-ion concentration of the superficial layer of water. Sprayed *chloropicrin* vapour kills larvæ in half an hour. This is suffocating and lachrymatory, must be handled in the open by trained operatives, and sprayed from large bottles not requiring to be often refilled. It is the most destructive larvicide of the "safe" agents so far employed. Usually a parachute containing the materials from which the gas or vapour is to be evolved is let down to near the surface of the water and opened, thus shutting off the surface from the rest of the well. To kill imagines simultaneously with larvæ and pupæ the well is closed and a dose of the culicidal gas introduced into the upper part of the shaft.[1]

There is scope for much ingenuity and a great deal of experimental work in India in connexion with this subject.

Aquatic vegetation in relation to mosquito larvæ.—All grass and weeds (except the various species of Lemna and Anacharis that grow in open waters) foster the breeding of mosquitoes by giving the larvæ shelter and protection from their enemies. The removal of all such vegetation from the surface and margins of collections of water—ponds, pools, tanks, banks of streams, etc.—is therefore important.

Lemna (aquatic plants popularly known as "duck-weeds"), of which two species are commonly met with, *L. minor* and *L. gibba*, are decidedly unfavourable to the breeding of mosquito larvæ when they form a thick covering, as they usually do. Where tanks or ponds are only partially covered with them, anopheline larvæ may, however, be found breeding prolifically; they should, therefore, either be removed altogether or their growth encouraged.

Anacharis, or American duck-weed, occurs also in a few tanks and permanent collections of water as a delicate, much-branched water-plant which is unfavourable to the breeding of anophelines. Its growth is usually so thick that the larvæ cannot move about the surface nor reach the bottom.

The *singhara* or water-nut plant (*Trapa bispinosa*), when the leaves cover the water thickly, is to some extent unfavourable to mosquito-breeding. When, as is usually the case, the plant does not grow up to the edges of tanks or other collections of open water, or when it has been removed from the margins, anophelines may be found in great numbers. It is probable that the stems and rootlets of the *singhara* plant greatly interfere with the movements of

[1] For an excellent account of many ingeniously devised experiments for preventing mosquitoes breeding in wells, see Report by K. B. Williamson, M.A., D.I.C., late Captain R.A.M.C. (T.F.), "The Use of Gases and Vapours for Killing Mosquitoes Breeding in Wells," contained in *Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XVII, No. 8, February 21, 1924, pp. 485–519.

fish. In some such ponds, however, small fish may be seen. The writer has observed that, of two tanks fairly adjacent, one densely covered with *singhara* and the other only partially covered, in the former there were no anopheline larvæ, in the latter there were swarms; the physical conditions of both tanks were otherwise, as far as could be noticed, identical.

Algæ, even when disposed in a moderately thick layer over the surface of collections of water, do not appear to affect the breeding of anophelines. *A. barbirostris* and *A. nigerrimus* appear to favour water containing these thallophytes more than other anophelines.

The water-lily (Nymphæa) does not appear to affect in any way the breeding of anophelines.

The tropical aquatic fern called "Azolla" has been recommended as destroying larvæ in their breeding-grounds. This is said to have the property of "spreading so rapidly that stagnant and running water in which it is planted is completely covered in a very short time." Small organisms such as mosquito larvæ, which require atmospheric air, are thus suffocated. Aquatic animals proper are said not to suffer any harm. It is not stated whether it is easy to eradicate the fern if so desired subsequently. It grows pretty freely on many of the tanks in the plains of India. It will grow quite well in any tank or very gently flowing water, and does not require any special treatment, except perhaps the removal of other aquatics from the tank. It will not grow in drains or small pools. "We are ready to send small quantities of this fern wherever you wish to experiment with it. But we personally have very little faith in its efficacy for suppressing the mosquito over anything more than a very limited area" (Memorandum by Superintendent, Botanical Gardens, Calcutta).

A curious method of destroying mosquito larvæ was described some years ago by S. DE PUYBERREAN. By cutting the leaves of a prickly cactus (*Opuntia vulgaris*) and steeping them in water a mucilaginous liquid appears on the surface in a few minutes. This liquid, poured into water, is said to act in a manner similar to petroleum; when pieces of the plant are simply thrown on the surface of the water a similar liquid forms, although it is slower in its effects.

The floating tufts of leaves of the water lettuce (*Pistia stratiotes*), whose rootlets harbour the larvæ of *Mansonia* and *Ædeomyia*, form a protection for some anophelines. It is widely distributed in India and is not easy to eradicate.

Eradication of aquatic vegetation.—The removal of all water weeds (except those mentioned as hindering breeding) from the surface and margins of collections of water is important. A few species of Anopheles may breed in water without visible vegetation, e.g. *A. barbirostris*, but all prefer some sort of vegetation for cover or food.

Of the many ways of treating surface waters against larvæ in different localities, it will usually be the case that in any particular locality one will be found by experience to be most convenient, suitable, economical and effective, and will be adhered to.

Scooping out of larvæ from ponds, etc.—In small ponds it is sometimes easy to deal with larvæ by brushing them out with a broom, or scooping them out with a tin attached to a long handle on the bank to get the full effect of the direct rays of the sun, which soon kills them. In streams with pools it is easy to brush them out along the bank, or drive them into the middle of the stream, where fish and other enemies may assail them. Netting larvæ is a laborious process and on the whole cannot be recommended.

Destruction of the food of mosquito larvæ.—As we gather more information regarding the life-history and bionomics of larvæ it is possible that our destructive measures may be extended to their food-supply. It is well known that in some ponds and small collections of clear water covered with weeds we fail to find Anopheles larvæ. It is considered that deep shade keeping off sunlight, by lessening the chlorophyll-containing organisms, renders waters unsuitable to larvæ.

Weeds, algæ, and lower forms of vegetable life generally, may be prevented from growing in comparatively small irrigation and other water channels by the use of a solution of sulphate of copper kept in metal cans, and pro-

vided with an automatic dropper. The strength of the solution required is about 1 pound to 10 gallons of water. This is an important auxiliary anti-larval measure, as algæ, and the lower cryptogams, afford both food and protection to larvæ. But $CuSO_4$ solution of larvicidal strength renders water unfit for man and animals, and this precludes its use in India.

C.—DESTRUCTION OF MOSQUITO LARVÆ BY FISH IN INDIA[1]

General Remarks.—Fish control, where it is applicable, is one of the most effective and economical methods of waging war against the mosquito. The experience of those who have fought this fight in the United States has been most satisfactory. W. E. HARDENBURG says:[2] "Once a natural breeding-place, such as a lake or stream, is stocked with the proper kind of fish, about the only work required to maintain their efficiency is occasional cleaning of its edges. In certain artificial breeding-places, such as fountains, underground cisterns, etc., even this is not required. Even where such cleaning is necessary, it has been the writer's experience, however, that in the long run fish control is cheaper and easier than oiling and ditching." In large, shallow ponds, borrow-pits and excavations containing Anopheles larvæ, where drainage is sometimes not feasible, and oiling is costly and laborious, fish control is often the very best way of dealing with mosquito-breeding. For shallow wells, certain kinds of cisterns, culverts holding water permanently, it is the most effective method. Alone, or in combination with *katcha nullahs*, fish control is sometimes the best and cheapest method for ditches and for small streams with a *continuous* flow of water, for certain marshes, swamps and pools, and other similar places (Figs. 79, p. 325; 80, p. 326; and 83, p. 337).

Pisciculture for anti-mosquito work has been raised to a fine art in some countries; in the United States it is looked upon as one of the three great anti-mosquito measures, complementing drainage and oiling. In India fish control of mosquitoes has not as yet advanced beyond the elementary stage. It is a valuable method of defence that should be developed throughout that country. The special virtue attaching to it is its cheapness as compared with the other anti-mosquito measures.

But fish control of mosquito-breeding has its limitations. It is, for instance, not applicable to one of the most frequent sources of mosquitoes in India, rain-water pools, since these soon dry up (and re-form), and the fish would die. It cannot, so far as the writer can see, be applied to rice-fields. Nor is it sufficient merely to stock a breeding-place with larva-eating fish and then depend on them alone; they require our assistance in certain ways from time to time.

Several writers have given us highly interesting accounts from observations of the manner in which fish destroy mosquito larvæ, and of the marvellous self-protective instincts in escaping from fish shown by these insects.[3]

Larvivorous Fish of India.—The family Cyprinodontidæ, group Carnivora, has many larva-eaters, and in India several members of the genera Pœcilia, Gambusia, Haplochilus, Cyprinodon and Fundulus are useful in this respect. Other families likewise contain larva-eaters, especially in the genera Ambassis, Trichogaster and Barbus.

[1] The writer is indebted to T. SOUTHWELL, late Director of Fisheries to the Governments of Bengal and Bihar and Orissa, for much of the information contained in this section. His essay, "Fish and Mosquito Larvæ," contained in *Annals of Trop. Med and Paras.*, Vol. XIV, No 2, 1920, is the best on the subject the writer knows of He is indebted also to W. E. HARDENBURG's *Mosquito Eradication*, and Col. A. B FRY's "Indigenous Fish and Mosquito Larvæ," contained in *Paludism*, 1912, No. 5

[2] *Mosquito Eradication*, p. 172.

[3] HILDEBRAND, *Fishes in Relation to Mosquito Control in Ponds*, U S Bureau of Fisheries, 1919.

The following species, which are mosquito-larva-consumers in natural conditions, occur abundantly in fresh waters in India

Genus *Haplochilus*. The species are small, the adult seldom over 3 inches long The dorsal fin is farther from the head than the elongate anal. The genus belongs to the group Carnivora, family Cyprinodontidæ, and to the sub-order Haplomi. There are four species:

1. *Haplochilus panchax* Ham. Buch. Occurs all over India, especially in Lower Bengal, Orissa, also in Burma, the Andamans, and abounds in all dead rivers and swamps. Attains a length of 3½ inches. Head flat, and fin has fifteen to seventeen rays. Lives on the surface of the water A nearly related Indian species is *Cyprinodon dispar*, which is a voracious feeder on mosquito larvæ; in fact, much superior to "millions" as a destroyer of mosquito larvæ Dorsal fin of *C. dispar* is nearer the head than the anal.

2. *Haplochilus melastigma* McClell. Smaller than preceding, attaining to a size of 1½ inches; anal fin has twenty to twenty-four rays. Widely distributed in India, especially in the Madras Presidency, Lower Bengal and Orissa; abundant in dead rivers and swamps.

3. *Haplochilus lineolatus* Cuv. and Val. Grows to 4 inches long; has vertical black bands. Occurs plentifully, especially in Coorg, the Wynaad, down the Malabar Coast and in Ceylon.

4 *Haplochilus rubrostigma*. Has a prolonged ventral ray spotted with red; attains a length of 3 inches. Found on the Malabar and part of the Coromandel Coasts.

All four species are hardy and breed freely in confined waters. They devour mosquito larvæ in nature with exceptional avidity.

Indian species of less importance are:

Ambassis nama Ham. Buch. Length 2 to 3 inches; breeds freely in confined waters; occurs abundantly

Ambassis ranga. Smaller than the above, but alike in habits; is not a surface feeder.

Trichogaster fasciatus Bl. Schn Attains to 4 or 5 inches in length. Occurs in both fresh and brackish water. Widely distributed in India. There are several varieties.

Badis badis Ham. Buch. Lives in mud; is very voracious; occurs in fresh and brackish water. Attains to 4 or 5 inches in length.

Barbus phutunio Ham. Buch. Length 1 to 2 inches; breeds in tanks. There are three other species of the genus *Barbus*, but their distribution is limited.

Other species occasionally act as mosquito-larva-consumers, e.g. *Perilampus* spp., *Barelius* spp., *Danio rerio*, *Rasbora daniconius*, etc Doubtless many other mosquito-larva-eaters remain to be discovered.

The *chilwa* (*Chilwa argentia*) has the reputation of being a destroyer of mosquito larvæ, and possibly it is so in certain circumstances, but the writer has on two occasions found anopheline larvæ in cisterns and tanks that had been stocked with chilwa.

Goldfish are sometimes useful larva-eaters in confined waters, but of no anti-mosquito value in large bodies of water. The sacred wells and tanks of India, often stocked with goldfish, seldom contain mosquito larvæ, and would probably contain none were they kept free from vegetation and débris.

From this brief account of the larvivorous indigenous fish it will be recognised that importation of other species is supererogatory. *Pœcilia* (Giradinus) *pœciloides* de Filippe, known as "millions," is a native of the West Indies and Central and South America. It was introduced into Ceylon a quarter of a century ago as a mosquito-larva-eater, but has since died out. It was also introduced into India by the Government of the United Provinces twenty years ago, and several specimens were sent to the tanks in the Zoological Gardens in Calcutta; hatcheries of them were also established in a number of other places, but it seems that they did not thrive and multiply. This small viviparous fish devours mosquito larvæ voraciously.

Development of fish control of mosquitoes.—The first step is to find out the most useful local species of larva-destroying fish that can be employed in anti-mosquito work. The nature of the collections of water in which each of these species is most effective should be determined.

The next step is to create an *aquarium* or *hatchery* in order that an abundant supply of fishes will always be available for stocking purposes. The species best adapted for destroying mosquito larvæ should be bred in confined areas, otherwise they will die out unless replenished from year to year. Usually a small, clear, shallow pond can be found for the purpose. It should not be so large as to make catching the fish difficult; nor should it communicate with a stream liable to flooding and consequent dispersal of the stock. The aquarium should be free from piscivorous fish. It is suggested that some of the indigenous mosquito-larva-eating fish resemble *Gambusia affinis* in the United States in being cannibalistic; hence one corner of the aquarium should be screened off with a $\frac{1}{10}$-inch wire netting to serve as a refuge for the young.

Local fishermen should be prevented from netting the fish as bait. The people should be informed as to the purpose of the aquarium, and a few placards should be posted on the subject. The aquarium should be stocked with selected larva-consuming fish netted in neighbouring streams or swamps, being careful not to remove too many, so leaving these places defenceless against mosquitoes. The number to be stocked in the aquarium will vary with its size, with the requirements of the area to be provided for, and the prevalence of these fish in the local sources. They are very prolific, and multiply with great rapidity if many pregnant females are initially stocked. If the aquarium is small and the number of fish in it very large, they will require to be fed. Chapatties made of maize or atta and minced fish answer the purpose.

The fish should be quite sound when added to the water; the container should receive sufficient air to support the fish, and be protected from the sun, small recesses in the reservoir for the fish to retire to when frightened are necessary—three slabs of stone, two standing on edge and one lying flat on the upper edge of these two, next a wall of the reservoir, form an effective retreat.

Number of fish required.—As soon as the aquarium is established, and the organisation for distributing the fish is completed, their dispersal to the places where they are required should be commenced. In this connection it is essential to know how many fish are necessary in each of the different kinds of breeding-places in order to prevent mosquito production. HILDEBRAND,[1] quoted by W. E. HARDENBURG in his *Mosquito Eradication*, states with reference to ponds: "The size of the pond must be considered; whether or not it is subject to wave action is very important; and the presence or absence of enemies of other larvæ-eating fish must not be overlooked. Even then we can only make a guess, for anopheline mosquito larvæ, at least, breed much more prolifically in some ponds than they do in others, for reasons not understood. It has been shown that a small number of minnows freed badly infested pools of mosquito larvæ in a short time; also that they destroyed the mosquito larvæ in ponds, and kept the ponds free of the aquatic stages of the mosquito, unless protection was provided by plants and débris. From the knowledge which has thus been gained we may conclude that, if a pond furnishes little or no protection for mosquito larvæ, a small number of top minnows is sufficient, but if it does furnish protection, a much larger number is desirable. Anti-mosquito work, however, may be started with a very small number of *Gambusia* [in India substitute prolific females, such as *Haplochilus panchax*], for this fish multiplies rapidly. There appears to be no danger of over-stocking, as observations indicate that the more fish a pond supports the more certain are the practical results." The same considerations apply to the fish control of streams, ditches, swamps and marshes. Brick or concrete cisterns containing, say, 1,000 to 10,000 gallons of water require from two to twenty fish, depending on the degree

[1] *Fishes in Relation to Mosquito Control in Ponds*, U.S. Bureau of Fisheries, 1919.

of infestation and other factors. The heat often reached by the water in metal containers kills the fish.

Low-lying culverts containing water permanently require fish; they are here most successful.

Large, shallow wells are soon cleared of larvæ if five to ten male *Haplochilus panchax* are introduced; two are sufficient for an ordinary village well, especially if it fills from below; two also keep a fountain free from mosquito larvæ;
two are sufficient for a garden cistern, angable to remove such growth. This
be periodically inspected, as the drawei a boat, but in most cases it is easiest
of water sometimes remove the fish, aible, toothed strip of steel 100 or more
not knowing why they are there do inf aquatic plants successfully, provided
replace them. irush or stumps. "The best implement

Distribution of the fish.—A nmsen saw. A similar but less effective
sponsible person must be placed in char-in ' wire used in the combing process
of the collection, distribution and caed. The wire is like a single-edge saw.
of the fish in their permanent quarte principle of a cross-cut saw, the men
A useful net for collecting top minnows re is a current the work is commenced
a small bobbinet seine. A net abs up-stream; the cut-off growth floats
12 feet long by 3 feet deep is a good ted ashore. If there is no current it is
If made of good material it is light wind, if there is any" [1] One, or at most
durable, and can be easily handled. ifficient. Repeated sawing is reputed to
dip-net, also made of bobbinet, maints. Tanks can be rendered free from
used satisfactorily in places where t steep cut and free from weeds and grass.
are so many roots or so much vegetvalue as mosquito-reducers, we have much
that a seine net cannot be used At the fish that are consumers of mosquito
any receptacle will do for the transpowhich they can act most effectively.
fish, and any convenient vehicle. rge ponds have an important place in the
small town the vehicle that carries r in the Bengal and Madras Presidencies,
the oil may be used on certain day thes, watering animals and other purposes.
carrying fish. emoval of earth for building the villages,

In many of the inland Southern Stth water by rain, land springs or subsoil
U.S., most large collections of water acti the present state of rural sanitation be
breeding-places are stocked with mosqe writer has not often met with Anopheles
larva-destroying fish, and it is found; found in most of them. Many of these
new stocks are seldom required, but d up, foul, and choked with weed and are
fish have to be helped by removing ve
tion and other floating matter, which seonds except to keep them free from weeds
to conceal the larvæ from the fish, uto-larva-eating fish. The pond cannot
prevents them from reaching the larvæ call fish, renders the water objectionable
though the larvæ be visible. "It is verpsented by the village people. *Singhara*
top minnows learn to follow the workmen engaged in cutting and raking vegetation from ponds. They soon become quite tame, and schools of them work almost under the tools of the labourers catching mosquito larvæ and other insects as quickly as their hiding-places are destroyed." [1] But all aquatic plants do not afford larvæ and pupæ cover against fish. Plants with straight stalks, grasses, and reeds without submerged leaves, afford no protection. Plants which hang over into the water should be removed.

Much care is required in the introduction of young fish, for in a promiscuous collection there are likely to be many of the predatory kind; pure fry must be used.

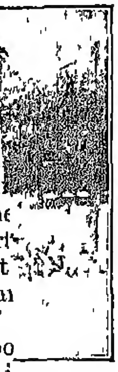
The writer is of opinion that the greatly extended use of mosquito-larva-

[1] HILDEBRAND, *Fishes in Relation to Mosquito Control in Ponds*, U.S. Bureau of Fisheries, 1919.

eating fish on the lines laid down in this section is a potent auxiliary in anti-malarial work in India. He is familiar with the many difficulties connected with giving effect to this recommendation, but these same difficulties existed in the United States and in other countries which have adopted fish control, and have been gradually overcome. It was in the actual carrying out of this method that the antecedent causes of failure were ascertained and the remedies discovered. He is also acquainted with all the objections that have been

writers and workers, but is strongly of
digenous mosquito-larva-eating fish preponderating that there should be no
States in being cannibalistic; hence ly in India. Figs. 79 and 80 illustrate
screened off with a $\frac{3}{16}$-inch wire nettir allowing odd water containers to lie about.

Local fishermen should be preven rva-protecting plants.—Larvivorous
people should be informed as to the pu he removal of all algæ and other larva-
should be posted on the subject. The protecting plants. It is
larva-consuming fish netted in neigh necessary first to get rid
not to remove too many, so leaving th from the shallow water's
The number to be stocked in the edge of all vegetation, so
requirements of the area to be provide attractive to Anopheles.
the local sources. They are very pr This can usually be best
if many pregnant females are initially done by a long-handled hoe,
the number of fish in it very large, tl or a shovel, thus leaving a
made of maize or atta and minced fish a clean edge devoid of any



The fish should be quite sound whe material which can conceal
should receive sufficient air to support larvæ from the fish. This
sun; small recesses in the reservoir for t cleaning of the edges may
necessary—three slabs of stone, two stai frequently be inexpensively
upper edge of these two, next a wall of done by lowering the water 6

Number of fish required.—As soo to 12 inches. The new shore
the organisation for distributing the fish i ates the border will be quite clean.
where they are required should be comme aquatic If there be areas of vegeta-
to know how many fish are necessary in phelines, tion out of the reach of the
places in order to prevent mosquito p ich keep hoe or shovel, it may be
W. E. HARDENBURG in his *Mosquito Erac* sufficient to oil these places
"The size of the pond must be consid tion. freely once a week. Such
wave action is very important: and t
other larvæ-eating fish must not be giving away fish, whose aid in the larva
make a guess, for anopheline mosquito
lifically in some ponds than they do in nsiderable protection from fish, and give
has been shown that a small number o aquatic grasses (*Hydrochloa* spp.), mosses,
mosquito larvæ in a short time; also nature Aquatic grass grows in shallow
in ponds, and kept the ponds free of t has many slightly submerged leaves over
which the horizontally floating or swimming Anopheles larvæ hover, out of sight and out of reach of the fish Wherever this plant occurs some Anopheles larvæ are almost sure to be present, regardless of the abundance of top-feeding fish.[1] This plant must be removed from ponds in which mosquito control is desired. This may be done by cutting and raking it, or, if growing in soft mud, by pulling it up by the roots. A species of this grass is to be found in most shallow tanks and ponds in India (see Figs. 43, 44).

Another great obstacle to fish is detached floating moss, met with in a large percentage of tanks. It has to be removed periodically when it is blown shorewards by the wind. Algæ frequently form floating mats near the surface which protect Anopheles larvæ from fish. Oil can be quickly and conveniently sprayed on the algæ, it is most effective, and in moderate quantity is not harmful to the fish; the algal pads act like sponges, retaining the oil and making them uninhabitable to

[1] HILDEBRAND, *Fishes in Relation to Mosquito Control in Ponds*, U.S. Bureau of Fisheries, 1919.

mosquito larvæ. $CuSO_4$ (1 pound to 10 gallons of water) will kill algæ, but it has to be repeated frequently. Water lilies do not afford much protection while growing. Some of the plants or their leaves, however, die every now and then, and sink in the centre, the edges adhering to the surface Mosquito larvæ find the cup thus formed and are then safe from fish. Later the dead leaves become detached from the main *plant, drift shorewards and cease to afford any protection to the larvæ.*

Sub-aqueous vegetation.—Extensive vegetation beneath the water seriously impedes the movements of fish and interferes with their function as larva-destroyers. It is generally advisable to remove such growth. This may be done by sickles and scythes from a boat, but in most cases it is easiest with a sub-aqueous saw This is a pliable, toothed strip of steel 100 or more feet in length; it will cut many kinds of aquatic plants successfully, provided only that the water is not studded with brush or stumps. "The best implement of the kind appears to be the patented Zeimsen saw. A similar but less effective saw may be improvised from the 'licker-in' wire used in the combing process in cotton mills, whence it may be obtained. The wire is like a single-edge saw. The sub-aqueous saw is worked on the principle of a cross-cut saw, the men pulling alternately on each end. If there is a current the work is commenced at the down-stream end and continued up-stream: the cut-off growth floats out of the way, is collected and hauled ashore. If there is no current it is preferable to cut in the direction of the wind, if there is any."[1] One, or at most two, sawings each season should be sufficient. Repeated sawing is reputed to destroy completely many of the plants. Tanks can be rendered free from Anopheles larvæ by keeping the edges steep cut and free from weeds and grass.

Before we obtain their maximum value as mosquito-reducers, we have much to learn about the habits of many of the fish that are consumers of mosquito larvæ in India, and the conditions in which they can act most effectively.

The village pond.—Tanks or large ponds have an important place in the life of the Indian villager, especially in the Bengal and Madras Presidencies. They are used for bathing, washing clothes, watering animals and other purposes. They are the excavations made by removal of earth for building the villages, and are kept filled or partly filled with water by rain, land springs or subsoil water. The village pond cannot in the present state of rural sanitation be abolished; nor is this necessary. The writer has not often met with Anopheles larvæ in them, but culicine larvæ are found in most of them. Many of these ponds have become more or less silted up, foul, and choked with weed and are good breeding-places for culicines.

Very little can be done to these ponds except to keep them free from weeds and grass and stock them with mosquito-larva-eating fish. The pond cannot be oiled; for oil tends to kill the small fish, renders the water objectionable for domestic purposes, and would be resented by the village people. *Singhara should not be removed; it forms part of the villagers' food.*

D.—DRAINAGE AND REGULATION OF SURFACE WATERS AS ANTI-MOSQUITO MEASURES

Drainage.—Vast areas throughout the world which were at one time endemically malarious have been freed from malaria to a great extent, while in some such places it has disappeared altogether. These satisfactory changes have been mainly effected by drainage and cultivation of the soil, by which the breeding-places of mosquitoes have been reduced, and with the consequent decrease of malaria the agricultural labourer has become more efficient, and

[1] HILDEBRAND, *Fishes in Relation to Mosquito Control in Ponds*, U S. Bureau of Fisheries, 1919.

able to produce more for the work put into the soil. The result is health and prosperity, better food and clothing, more comfortable habitations, better educational facilities—in short, a rise in the physical and mental standards of agricultural communities, who have been put into the position of being able to help themselves. There are now many precedents for reclamation of extensive *uninhabited areas* for agricultural purposes—large tracts in North, Middle and South America, Algeria, Federated Malay States, etc.—and Dr. W. E. DEEKS[1] puts the question, "Is it not just as commendable, and infinitely more humanitarian, to spend money for the reclamation of large *inhabited areas*, and thus reclaim, not only the land, but the inhabitants also?"

For many years the writer has been surprised that so little has been done, and so little written, about anti-mosquito measures in India; although destruction of malaria-carrying Anopheles is incomparably the most important anti-malarial measure, since it breaks the main link in the chain of the cycle of the malaria parasite. At the Bombay Medical Congress of 1909 the possibility or practicability of anti-mosquito sanitation as a means of fighting malaria in India was almost ridiculed. To-day this uncompromising attitude is no longer adopted. Within the present generation quinine or cinchona febrifuge is not going to eradicate malaria from India. The fact is, in general, insufficiently stressed that malaria is essentially a local disease. If all the anopheline breeding-places of a locality are abrogated, the Anopheles of another place miles away will not immediately re-introduce malaria.

It is not the case (as has been supposed, to the detriment of local anti-malarial work in India) that it is hopeless to attempt to eradicate Anopheles because immigration from neighbouring places would neutralise the effects of the good work done. Had this view been acted on, the Panama Canal would not have been built, Algeria would have remained a desert, Italy would not have had its malaria so enormously reduced, and in other regions, where it is now absent or very mild, malaria would still be rampant. A great deal of mischief, also, has arisen from the fact that it has been repeatedly stated that mosquitoes can be easily and cheaply eradicated, whereas it is usually a costly and laborious undertaking, and when Governments find that it is both laborious and troublesome, they are disgusted and disappointed.

Prof. CARL PEARSON has shown, on mathematical grounds, that if mosquito propagation is suppressed within a *circular* area of 1 mile in diameter, the mosquito density at the centre will be 3 per cent., at ¼ of a mile from the centre 18 per cent., and at the periphery 75 per cent. of the density of the surrounding area. A *square* mile of area will have a central density of 2 per cent., at ¼ of a mile from the boundary 11 per cent., and at the boundary 50 per cent. of the surrounding density. These figures can only be accepted in a broad general way. They are based on a number of suppositions with regard to the habits of mosquitoes regarding which mathematicians can have little knowledge; mosquitoes are not nuts. However, the writer's experience in the military cantonments of India and Burma has borne out the reliability of the above general statement. Reduce the Anopheles from the centre outwards and you reduce the malaria.

It is, then, necessary to deal with each locality as a separate problem.

There are areas in which a single species of Anopheles, having a special kind of breeding-place, is the only local carrier of malaria. Where this is so, abrogation of that particular type of breeding-place does away with the incriminated Anopheles, in proportion as it does not adapt itself to water collections of another kind. Let us consider a few such places.

[1] *Malaria, its Cause, Prevention and Cure*, p. 29.

Reduction of malaria-carrying Anopheles in the Federated Malay States.—The divergent local effect of drainage and clearing of jungle in the Federated Malay States is one of the most forcible proofs of the part played by Anopheles in malaria. These operations on the flat coastal lands have produced an almost miraculous disappearance of malaria over thousands of square acres, but were total failures on the hilly lands. On the *flat land A. umbrosus*, a malaria-carrier which breeds in pools in the jungle, is exterminated when these pools are drained even by open ditches. On the *hill land* the chief carrier is *A. maculatus*, "a mosquito which cannot be exterminated in the ravines by open drainage, however quick the current, since its proper breeding-place is the running water of springs and hill streams. . . . Since over thousands of square acres of flat land malaria has been abolished, so the manager of the hill estate can abolish the disease if he abolishes the breeding-places of the hill carrier by putting the water of ravines underground."[1]

The story connected with the eradication of malaria from the Old Seafield (rubber) Estate, F.M.S., resulting from subsoil drainage of springs and streams of ravines, as related by Sir MALCOLM WATSON, is one of the most enthralling accounts of anti-malarial sanitation carried out in the East. It is summarised in the following words: "What was probably as intensely malarious a place as exists on the face of the earth, one which for the Indian labourer was uninhabitable except at an unjustifiable cost of life, is now so free from malaria, although not completely free, that Indians come to it readily, a large and efficient labour force lives on it, and a further improvement in health may be anticipated with confidence."[2]

Malaria in the Andamans.—Lt.-Col. S. R. CHRISTOPHERS, C.I.E., O.B.E., F.R.S., I.M.S., has shown that in the Andamans a single species of Anopheles (*A. ludlowii*) is the sole malaria-carrier, that its breeding-places are limited to a half-mile-wide strip of coast-line and are not difficult to deal with. These islands, situated in the Bay of Bengal, in the direct course of the monsoons, have a heavy rainfall, and, with the exception of a cleared area at Port Blair and Aberdeen Island, are covered with virgin jungle. There is no reservoir of carriers apart from the convicts themselves, so that there exists a controlled population under discipline, and a very limited area to deal with, from which malaria can be altogether eliminated. The writer is familiar with the Andamans, and in 1912 repeated most of these observations. It is now known that open drainage is capable of abrogating *A. ludlowii* and eradicating malaria where this species is the only natural carrier.

Malaria in Bombay.—Lt.-Col. GLEN LISTON, C.I.E., I.M.S., from original observations, incriminated *A. stephensi* as the carrier of malaria in the city of Bombay. Dr. C. A. BENTLEY, in an extremely able report on the outbreak of malaria in Bombay in 1911, confirmed Liston's findings, and demonstrated that *A. stephensi* bred in the *private wells* in compounds, and that, if these wells were closed or filled up, the disease would cease. He suggested that not only could malaria be reduced, but that it could be "absolutely eradicated from the greater part of Bombay at a cost which would amount to less than a tenth part of the loss estimated to be occasioned each year by the disease."[3]

These instances show that we are gaining ground on the malaria-carrying insect. A more intimate study of the bionomics of the other known malaria vectors in the Indian Empire will greatly facilitate and cheapen our methods of dealing with them. The facts just detailed are most encouraging, and give us grounds for expecting that a time will come when we will possess much clearer ideas on the methods of reducing malaria-carrying mosquitoes than we have at present.

If any malaria vectors are strictly adapted to, or consistently adherent to, any collection of water so specially distinctive in character as to justify the

[1] Sir MALCOLM WATSON, *The Prevention of Malaria in the Federated Malay States*, 2nd Ed., p. 59.

[2] *Ibid.*, pp. 130–56. The writer would here acknowledge his special indebtedness to this book, which is a mine of wealth to the field malaria worker and medical administrator in India.

[3] *Paludism*, No. 4, March, 1912, p. 3. "Presidential Address" by Sir PARDEY LUKIS to the Committee for the Study of Malaria, Bombay, November 16, 1911.

limitation of preventive measures to waters of that particular kind, a line of direct attack is indicated. A specific preventive policy of this kind, if rationally established on fact, would be decidedly more economical than the more comprehensive one of attacking all anophelines. But with this specific preventive policy we are always up against the fact that anophelines, when deprived of their chosen breeding-place, will adapt themselves to the next best one available. *A. maculatus*, though having a preference for clear running water, can adapt itself to many conditions. The writer found larvæ of this insect in four different kinds of water in August 1909—in the open water-supply reservoir at Almora, in a roadside streamlet at Bowah (below Naini Tal), in the marshes below the Bhim Tal lake, and in the lake itself. We must, therefore, check our observations periodically, and likewise keep an eye on all potential breeding-places.

As Lt-Col S. P. JAMES, I.M.S., writes: "In each place we must study, not only Anopheles, not only the species of Anopheles, but the actual *infected* anopheline in the house." From these considerations, it must be obvious that exact biological research in connexion with the particular local species of Anopheles carrying malaria must be undertaken before any measures applied against it can succeed. The writer is filled with the hope that the time is not far distant when it will be possible to state definitely which are the special natural malaria-carrying Anopheles in every town, military cantonment, civil station, tea-garden, etc., and to show on the malaria map of each place where the infecting mosquitoes are breeding and feeding on man, and the progress being made towards the abrogation of the breeding-places.

General remarks.—Whatever place we are dealing with, we require clear and exact knowledge of the local conditions, obtained by preliminary investigation. If this rule is observed anti-mosquito measures will prove the most potent way of fighting malaria.

One of the factors that dominate anti-mosquito measures of the present day is the distance of flight of anophelines, because it is the area within the normal distance of their range of flight to which we direct attention in endeavouring to effect the destruction of their larvæ and to abolish their breeding-places. Certain carefully carried out observations in India have shown that the distance of flight is ordinarily not more than half a mile—this was the distance laid down by the Malaria Commission of the Royal Society of 1902; exceptionally they may fly much farther (p. 119). Usually the breeding-grounds of anophelines are within a quarter of a mile of the dwellings of the human beings they feed upon. Nevertheless some authorities have suggested that, during the very cold weather of Northern India, anophelines may yearly migrate *en masse*, to return when the meteorological conditions are more favourable. This has been observed in several other countries. In a recent case of such migration in Australia they came in clouds and were locally associated with an epidemic of dengue; then they vanished and the disease disappeared. The practical point is that the number of anophelines which in ordinary conditions operate in the dissemination of malaria at a greater distance than half a mile is probably so small as to be negligible. Marshes, *jheels*, irrigation canals, rivers, etc., at a distance from towns and cantonments are frequently incriminated as factors connected with local malaria without any foundation in fact, and in some instances large sums of money have been wasted in endeavouring to remove breeding-places that were not concerned with the local malaria.[1]

Wherever possible it is preferable to institute permanent rather than

[1] The characters of the breeding-grounds of the different species of malaria-bearing Anopheles met with in India have been dealt with in the section on ANOPHELINI OF INDIA, p. 126 *et seq*

temporary measures, and the most comprehensive measure is to lower the ground-water level by drainage. The next is the drainage of individual breeding-grounds, a method which can largely be employed in endemic malarial districts, often without any costly engineering works. The abolishment, complete or partial, of breeding-places of anophelines is the most generally useful measure, especially in isolated towns, cities, villages and houses. In such places all householders should be responsible for the absence of mosquito breeding-places from their compounds or premises. In every house in endemic malarial areas efforts should be made to abolish all breeding-places. Disused springs and wells should be covered or otherwise rendered inaccessible to mosquitoes, and every possible collection of standing water should be abolished. The banks of small streams should be kept properly graded and cleared of grass and weeds, so that no opportunity may occur for water-logging in irregularities, or for aquatic vegetation thriving. In areas with a limited number of breeding-places and a small rainfall, and where there are no irrigation canals, the doing away with breeding-grounds is a comparatively easy task. On the other hand, in some circumstances it may be impossible. "A year's careful study of the breeding-grounds in the suburbs of Calcutta showed that both the tanks, and still more the unlined roadside drains, aggregating to many scores of miles in length, also breed abundant Anopheles. It is quite impossible for municipalities to find funds for lining or levelling these drains, or to keep them continuously kerosened to destroy the larvæ; the attempts to do so having had to be abandoned in urban areas in Lower Bengal, while they are still more impossible in rural areas, which contain the vast majority of the teeming population of this part of India." [1]

Of the simpler anti-mosquito measures, the most comprehensive in its effects, and the most generally useful, is that of doing away with all stagnant collections of water in the neighbourhood of private dwellings, villages, towns, civil stations and cantonments by filling up hollows and irregularities or by draining them.

Anti-mosquito drainage, etc.—Anti-mosquito drainage usually includes the institution and maintenance of one or more of the following procedures: Ditching, plain or lined; subsoil tile drainage, vertical drainage and absorbing wells; re-channelling of water-courses; training and canalising wandering streams, water-courses, and sluggish waters generally, and control of irregular channels; taking streams underground; salt-water drainage, including dyking, construction of tide gates, prevention of silting, and pumping. In association, or not, with drainage we may have to carry out general surface levelling. This comprises the filling in of ponds, marshes, and all manner of irregularities of the surface; the removal of their waters by drains or cuttings, small, medium or large; the reclaiming and revitalising of swamps, attention to culverts and ditches; restriction of wet cultivation; regulation of the flow in irrigation waters; and regulation of drains alongside roads and railroads. In short, drainage includes all classes of work required to carry off and abolish open collections of water and to lower the subsoil-water level; it also embraces eradication of aquatic vegetation and clearing of all natural and artificial water channels. The malarial expert is therefore brought into intimate relation with such subjects as—meteorology, hydrography, topography, geology and sanitary engineering.

Drainage on a large scale.—On a large scale drainage is called for wherever the subsoil-water level is high or the soil water-logged, and where there are marshes or other large collections of water acting as breeding-places for anophelines. Drainage as part of public protection against malaria has, we know, been

[1] Sir Leonard Rogers, C.I.E., F.R.S., I.M.S., *Fevers of the Tropics*, p. 237.

practised for many centuries. In the *Report of the Italian Society for the Study of Malaria* for 1906 the opinion is recorded that "improvement in drainage should first be undertaken in a malarious locality: then improvement in agricultural methods, *i.e.* regular and careful cultivation; then should follow the new anti-paludal measures." This may apply to certain limited districts, but it is doubtful whether many medical officers of Indian experience would advise the application of such an important generalisation to our larger endemic malarial districts in India. From a scientific point of view it is possible theoretically, with great expense and labour, to drain towns and cantonments in India in such a way that malarial fevers would be considerably reduced. Practically it will prove impossible for many years to come to eradicate malaria from the huge agricultural districts of India, but it can be *reduced* almost everywhere.

Large areas of swamp and marsh lands have been rendered cultivable by proper drainage. Millions of acres of land in India to-day are not producing what they should because they are not properly drained. Money spent in anti-mosquito drainage is often rapidly repaid by the natural resources made available. In many places the wood cleared alone pays for the drainage.

All the larger works of drainage, canal-making, irrigation, etc., must necessarily be controlled and inaugurated by Government. The writer is convinced that Government would be ready and willing to spend money on sanitary measures if it could be definitely shown that they were able to prevent malarial fevers in communities. It is not easy for the sanitary officer in particular cases to state emphatically that the measures he recommends will unequivocally eliminate, or even mitigate, malaria. He can only base his opinion on the principles already stated, and use as illustrations the advantages obtained in certain districts in which anti-malarial measures of a like kind have been systematically carried out. Drainage of this magnitude is always a serious undertaking; even in small areas, drainage scientifically carried out means expenditure of funds which at first sight appears disproportionately high to the prospective results.

The question whether there should be greater State intervention in connexion with hydraulic sanitation as an anti-malarial measure throughout India is a problem which the writer does not here attempt to consider. It would appear that there are some districts in which such intervention could be profitably undertaken and the areas rendered less malarious. Even in cases where the conditions are favourable it would necessarily be a work of slow progress and great cost.

Large drainage schemes nearly always take some time to show any distinct influence for the better, and usually it is not until well into the second year that the number of admissions of malarial fevers is much decreased, this diminution becoming more marked by the end of the third and fourth years. In really comprehensive drainage works that take several years to carry out, it frequently happens that it is not until the work is approaching completion that malarial fevers are materially lessened.

The salutary effect on malaria which follows drainage of a previously malarial district is not entirely due to the drainage, for it is well known that drainage *per se* is an anti-malarial measure that takes a long time to operate beneficially. There are other factors, such as improved sanitation and water supply, better housing, healthier lives, general levelling of the surface, impermeable roads, abolition of collections of water that previously existed, and all the other attributes of industrial prosperity, that must be taken into account before we can estimate the intrinsic merits and influence of drainage alone. Whatever form of hydraulic sanitation is instituted in any particular locality must be undertaken in view of the present known endemiological and epidemio-

logical facts connected with malaria. "The essential requirement of all systems of hydraulic sanitation is that they do not leave a way for the larvæ and nymphæ of anophelines to live in the water" (CELLI).

There are instances in the history of malaria in various countries in which the initial stages of the drainage of marshes and malarial districts have been associated with outbursts of malaria of a virulent type. Such was the case in some of the drainage operations in England during the early part of last century, in certain parts of Italy between the Tiber and Arno Rivers, and in the terrible effects of the drainage of the marshes near Chartreuse in 1805, which it is recorded led to 12,000 cases of pernicious malaria with 3,000 deaths.

Drainage schemes of any dimensions require the technical knowledge of a sanitary engineer of some experience; if he has special knowledge of drainage in relation to malaria *tant mieux*. There is, of course, a decided difference between rural and urban drainage schemes. Anopheles are largely rural, hence urbanisation of areas tends to lessen them. The area to be drained should be inspected when at its worst, that is, during the heaviest part of the rainy season and flood times. Where the malarial season is well marked, the drainage scheme, or definite sections of it, should, if practicable, be commenced and finished in the interval between two malarial seasons. All systems of drainage, natural and artificial, require well-organised, efficient and constant supervision.

Principles of subsoil-water drainage.—The subject of subsoil-water drainage is so intimately related to the reduction of Anopheles, and consequently of malaria, that it is essential that sanitary officers working in India and executive and administrative medical malarial officers should be familiar with the principles underlying this form of drainage. This knowledge is as much part of their equipment as is the entomology of mosquitoes. They should also have a practical knowledge of the composition of the soil in so far as it is concerned with the holding up of surface waters, so fostering the creation of breeding-places for mosquitoes. The writer, therefore, takes this opportunity of referring to a few points of special interest in this connexion.

Particles of soil are surrounded and bound together by a thin film of capillary water. It is this film that allows of damp sand being moulded into masses, which crumble when the sand dries. The film is extremely thin, and does not move through the soil in the way subsoil water does. When more water reaches the soil, say by rain, flooding or seepage, the film over the particles of soil becomes thicker; this excess can move upwards or downwards; upwards when evaporation is in progress, downwards to the subsoil water and to drains when the soil is drained. If still more water reaches the soil the excess passes downwards until, at a varying depth, all the "pore" spaces (air spaces between the particles) are filled with water; this forms the surface of the water table, whose level varies with the quantity of water in the soil, the rainfall and natural or artificial drainage. "When the pore spaces are filled with water the thin film round each particle of soil no longer exists, the particles are no longer bound to each other by the surface tension of the film, and they may easily move on each other; hence wet sand is almost fluid, and swampy land is soft."[1] The malarial sanitarian is specially interested in the control of this surplus water.

In Fig. 81, II, when there is a drain at A and C only, the undrained soil must be highest at B, the point farthest from the drains; but if an additional drain is placed at D, then the highest levels of the water will be found at E and F. The water, as a whole, will then be farther below the surface and the land better drained.

The drained, dry soil above the water table forms a receiving space for

[1] SIR MALCOLM WATSON, *Prevention of Malaria in the Federated Malay States*, 2nd Ed., p. 265.

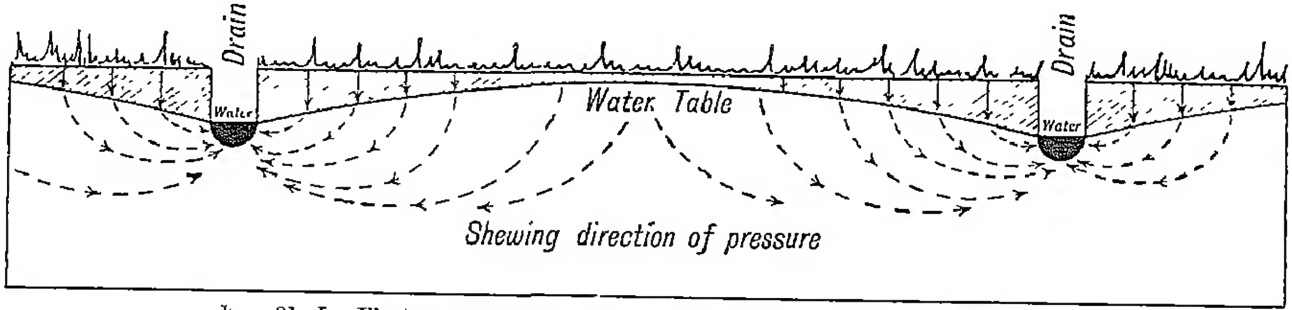


FIG. 81 I.—Illustrating the principles of subsoil-water drainage. (After SCOTT.)
From Sir MALCOLM WATSON's *Prevention of Malaria in the Federated Malay States*, 2nd Ed

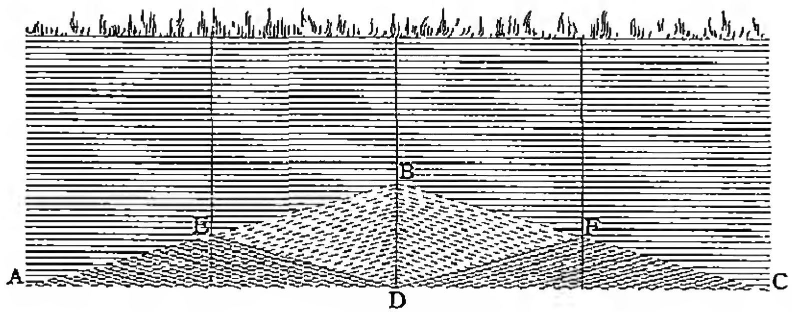


FIG 81, II.—Illustrating the principles of subsoil-water drainage. (After SCOTT.)
From Sir MALCOLM WATSON's *Prevention of Malaria in the Federated Malay States*, 2nd Ed

the rainfall, and prevents it forming pools, etc. Two feet of soil in most parts of India can absorb 8 inches of water.

Drainage carries away excess of water from the soil; air takes the place of this water, until the next fall of rain or flood, after which the drains once more remove the water, which is replaced by air. This aeration of the soil is of vital importance to the agriculturist. For the anti-mosquito sanitarian it allows the rain to be absorbed, instead of forming swamps or pools. Drainage tends to harden the soil; it allows man, animals and vehicles to move on it without creating deep impressions, which expose the ground waters and form mosquito pools.

Of the subsoil water which enters porous pipes laid some feet below the surface, about $\frac{1}{1500}$ part penetrates the substance of the pipes, the rest gaining access through the crevices between sections. Practically, the influence of porosity is so small that we may regard the whole of the water as entering the joints, but the greater portion, it must be remembered, does so from below. In a well-drained soil the subsoil-water level is at the level of the drain-pipes. When rain falls on the surface the water descends to the water table, which then begins to rise, and if the drains are sufficiently active, the pipes will carry off this rise of water as fast as it enters them from below. If the rainfall is greater than the pipes can remove, the drain becomes submerged below the water table; when it ceases, the flow through the drain steadily lowers the water table so that it may fall below the bottom of the pipes, the flow through which comes to an end (Fig. 81, I and II).

That the water will be freely admitted to the pipes at the joints is easily shown. With 2-inch pipes, when laid end to end as close as possible, the opening between two of them is usually not less than $\frac{1}{10}$ of an inch on the whole circumference This makes $\frac{6}{10}$ of a square inch opening for the entrance of water at each joint. In the length of a drain between any two points (say 100 yards' distance, with pipes 12 inches long) there will be 300 joints or openings, each $\frac{6}{10}$ of a square inch in area, or a total of 180 square inches for admitting water to the drain. The area of the outlet from a 2-inch pipe is, however, only about 3 square inches, so that the inlet area is nearly sixty times greater than the outlet area.[1]

These few paragraphs contain the secret of how the malaria of many agricultural districts in India, as well as towns, cantonments and civil stations, is to be reduced

Ditching and its application in anti-mosquito work.—The level of the ground water is lowered by various devices, the most primitive of which is the *earth drain* or *ditching*. These ditches are left open, or partly filled with stone, gravel, and finally earth. The open earth *katcha*[2] ditch is the form of drainage in general use in India. It has many disadvantages; if neglected for a few months it creates conditions favourable for the breeding of mosquitoes. It silts up, the sides crumble, irregularities of the bed are produced, the flow is dammed, vegetation covers the sides and bed, pools form. All this involves continuous expenditure in upkeep, levelling, removal of weeds, and supervision. But with all these disadvantages it is an invaluable method of drainage in India, especially in rural areas. In the vast majority of places it is the only one which can be considered feasible. *The construction of properly graded surface drains to suitable outfalls is initially the most comprehensive and economical means*

[1] SCOTT on "Drainage," quoted by Sir MALCOLM WATSON in *Prevention of Malaria in the Federated Malay States*, 2nd Ed., pp. 260, 270

[2] The term *katcha* (Hind.) is applied to anything that does not last—the impermanent, temporary, unstable, and the unsubstantial, e.g. the use of mud for building the walls of houses. The one factor always in favour of what is *katcha* is cheapness.

of reducing malaria-bearing Anopheles in India. Initially, no anti-malarial drain other than a ditch drain should be laid; the plain open *katcha nullah* is the most frequently employed anti-mosquito drain in use in all malarious countries. The cost is comparatively small. Fig. 82 represents a typical ditch; see also Figs 85, 86 and 88. One of the great advantages of open-ditch drains is that, if they are not deep enough, they can be lowered at comparatively little cost. If a *pukka* drain is laid too high, it is of little use in reducing the level of the subsoil water, and to lower it is as costly as laying a deeper drain or lower subsoil tile drains. The level of the outlet is always most important, especially at the sea-coast (see Fig. 99, p. 350). In the latter case the opening should be at the lower level of neap tides.

An open drain in flat land, if deep enough, will reduce the breeding-places of Anopheles on the area it drains, and thereby the malaria carried by them

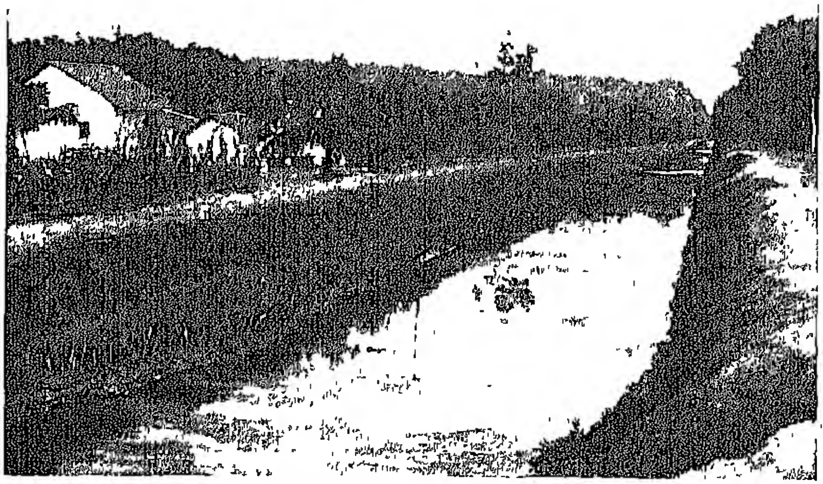


FIG. 82.—A large agricultural drain in flat land.

From Sir MALCOLM WATSON's article, "Mosquito Control," in BYAM and ARCHIBALD's *Practice of Medicine in the Tropics*, Vol. I.

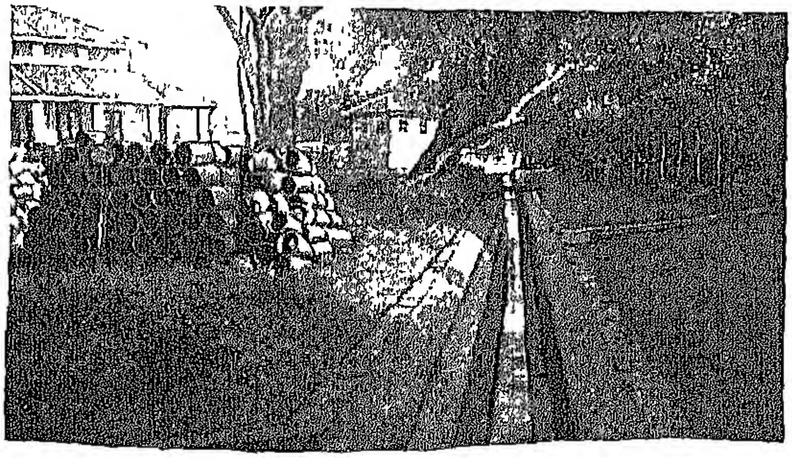
(Figs. 82, 87 and 88). Its existence does not interfere with any better means of draining the land that may be devised later. At some future date it may be possible to substitute either underground pipe drains or brick drains for open drains, and thus do away with the upkeep of open-ditch drains.

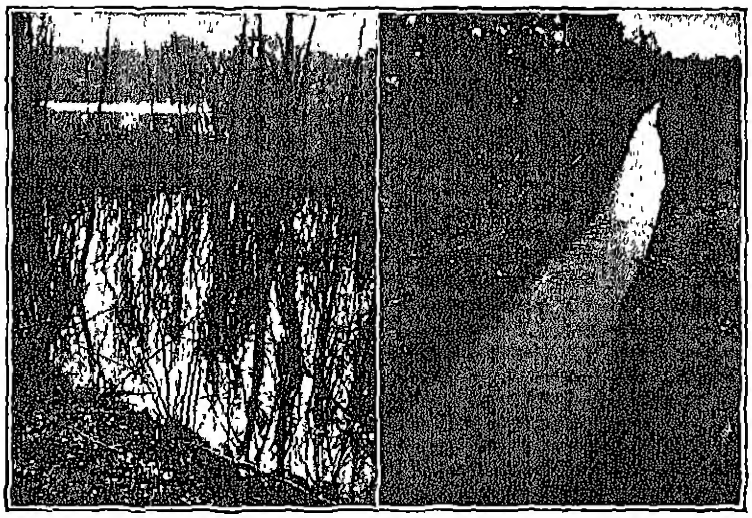
The *katcha* drain should be prevented from becoming a breeding-place. It should be kept to the established grade and proper cross-section, free from grass, weeds, floatage and débris generally.

Ditching may be necessary on hard, open land, when the cost is smallest: or in wooded swamp or marsh land, in which case the work is expensive. The methods of excavation will depend on the conditions. On hard, clear, open ground machinery may be used with advantage; in swamps some form of blasting may be cheapest. Only the smallest number of ditches that will effect what is necessary are to be made, and wherever possible they should have clean-cut

All ditches should be in good working order before the mosquito-breeding season begins, and maintained so during its continuance. Monsoon storms and torrential rains may ruin the gradients of miles of *katcha* drains, and create irregularities of the bed which may become breeding-places. In cases where the banks of ditches in pasture lands are flat and soft, both above and below the flood line, deep impressions, which hold water, are sometimes made by the hoofs of horses and cattle. Where practicable, such soft areas should be protected by fences, and a barrel without a bottom should be installed, or a large, bottomless, strong earthenware cylinder (*naund*) sunk to the surface level at a suitable place, where it will remain filled with water for animals to drink.

Permanent lining of ditches.—Anti-mosquito ditches may often be lined, with most satisfactory results, especially where excessive erosion takes place,





FIGS. 85 and 86.—Left, large cat-tail swamp fed by a spring; right, ditch dug to lead water around the swamp.

From HARDENBURG'S *Mosquito Eradication.*

of reducing malaria-bearing Anopheles in India. Initially, no anti-malarial drain other than a ditch drain should be laid. the plain open *katcha nullah* is the most frequently employed anti-mosquito drain in use in all malarious countries. The cost is comparatively small. Fig 82 represents a typical ditch; see also Figs 85, 86 and 88. One of the great advantages of open-ditch drains is that, if they are not deep enough, they can be lowered at comparatively little cost. If a *pukka* drain is laid too high, it is of little use in reducing the level of the subsoil water, and to lower it is as costly as laying a deeper drain or lower subsoil tile drains. The level of the outlet is always most important, especially at the sea-coast (see Fig. 99, p. 350). In the latter case the opening should be at the lower level of neap tides.

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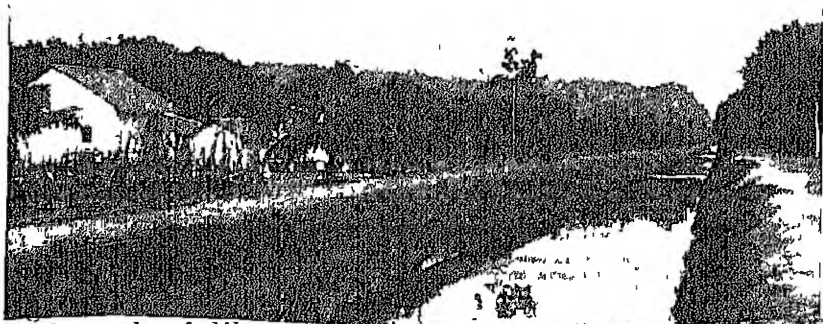

posit of silt, sand and débris at the point of union (Fig. 87).

The alignment of all extensive or important ditches should be done by the engineer himself. He will require an efficient staff of assistants and overseers. In India practically all *katcha nullahs* are made by hand; the schemes are usually on too small a scale to justify the purchase of machinery for excavating. In large drainage schemes, however, machinery is cheapest and quickest.

Ditching should not be employed without discrimination. There is little use in draining a pond that can be controlled for much less money by stocking it with fish. Nor will it pay to try to drain a swamp that can be protected at much less expense by means of dykes and flood-gates.

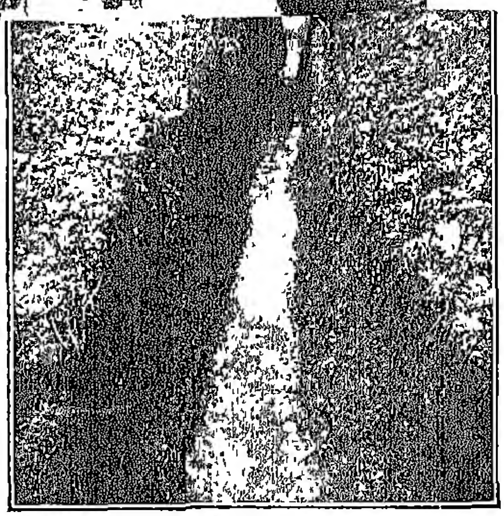

FIG. 88.—This open ditch, in places 15 feet deep, and more than a mile long, was dug by five Alabama farmers as a land-improvement project. It drained a swamp of nearly 50 acres. From HARDENBURG's *Mosquito Eradication.*

All ditches should be in good working order before the mosquito-breeding season begins, and maintained so during its continuance. Monsoon storms and torrential rains may ruin the gradients of miles of *katcha* drains, and create irregularities of the bed which may become breeding-places. In cases where the banks of ditches in pasture lands are flat and soft, both above and below the flood line, deep impressions, which hold water, are sometimes made by the hoofs of horses and cattle. Where practicable, such soft areas should be protected by fences, and a barrel without a bottom should be installed, or a large, bottomless, strong earthenware cylinder (*naund*) sunk to the surface level at a suitable place, where it will remain filled with water for animals to drink.

Permanent lining of ditches.—Anti-mosquito ditches may often be lined, with most satisfactory results, especially where excessive erosion takes place,

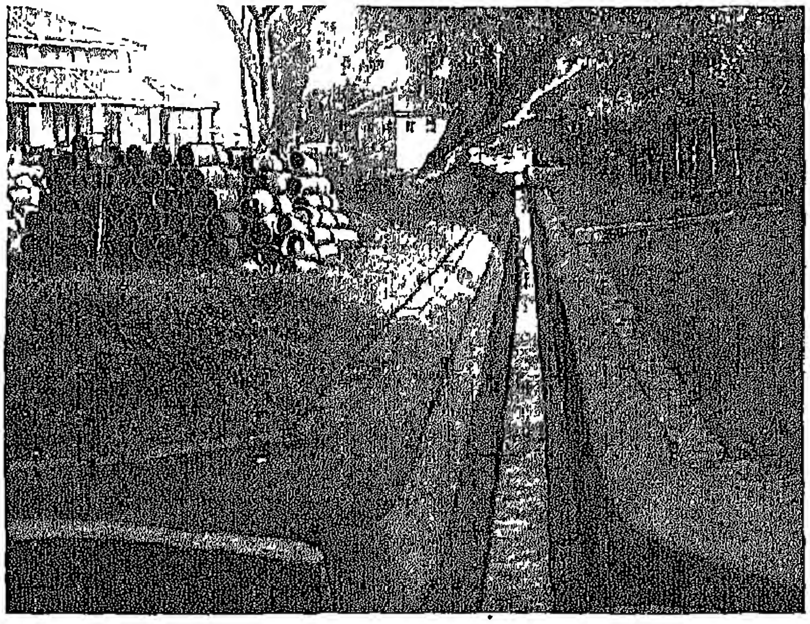

FIG. 89.—A large concrete drain with a narrow invert. At the side of the drain is a pile of subsoil drains.

From Sir MALCOLM WATSON's article, "Mosquito Control," in BYAM and ARCHIBALD's *Practice of Medicine in the Tropics*, Vol. I.

or where maintenance costs of *katcha* drains are exceptionally high (Fig. 89). The materials used for lining ditches are concrete, stone set in mortar, and planks. Concrete is the most costly, but also the most permanent. "Lined ditches are more permanent, easily cleaned, require less inspection and are ultimately less costly. At some of the settlements in the Panama Canal Zone it was found that a large saving was made by lining certain ditches and parts of ditches with concrete, as against repeated regrading, cleaning and oiling of open earth ditches."[1] (See Fig. 92, p. 340.)

The lining should be U-shaped with sloping sides; it is not always necessary, however, to line the whole depth of the ditch (Fig. 89). The lining of the bottom

[1] LE PRINCE, *Malaria Control Drainage as an Anti-Malarial Measure*, U.S. Public Health Service, Reports, 1915.

and sides up to 3 or 4 inches above the normal water line will generally answer for small ditches. In wide ditches the bottom should slope towards the centre, and the side walls may often be nearly vertical (Figs. 90, 91). A smooth, elaborate finish is not essential. The *nullah* may be lined roughly with flat stones, the holes being chinked up and mortar plastered about them. Where flat stones are not available a 2-inch layer of concrete, reinforced with chicken wire, may be used.

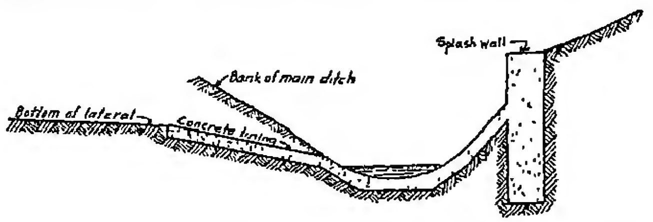

Fig. 90.—Cross section of lined main ditch and unlined lateral. (Modified after Le Prince.)

"In order to avoid scouring out of banks above the lining by storm water, particularly at sharp curves or bends of ditches, the outer wall lining should be raised to meet the condition, or the ditch may be widened or key-walls installed. Key-walls (Fig. 91) will prevent the side scour and under-scour of linings of straight ditches of heavy grades. The key-wall should extend 6 inches to a foot or more into the ground below the bottom ditch lining. Branch ditches should enter lined ditches at an acute angle or on a curve, with a sharp grade near the junction. In all cases weep-holes or seepage-holes, sloping towards the centre or bottom of the ditch and located just above the key-wall, should be provided. These are required to prevent the effect of currents which may be under or behind the concrete ditch lining. Weep-holes should be made in side walls before the concrete has set. They should be used wherever water might be behind the lining." [1]

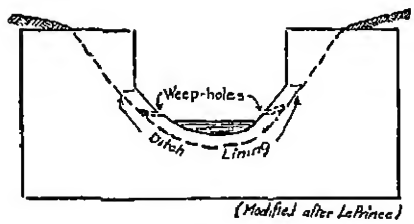

Fig. 91.—Cross-section of key-wall. From Hardenburg's *Mosquito Eradication*.

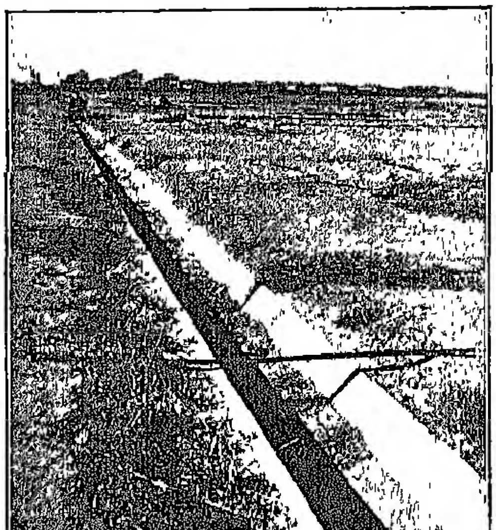

Fig. 92.—Open ditch lined with concrete. From Hardenburg's *Mosquito Eradication*.

Grouted ditches.—A noteworthy advance in anti-mosquito sanitation was the introduction of a system of shallow, open, cemented, plastered or grouted ditches, which is used with success in flat, marshy land. It is also a satisfactory method of dealing with the drainage of hillsides which have only

[1] Hardenburg's *Mosquito Eradication*, p. 127.

a gentle slope. "Grouted ditches are shallow, open channels made of hen-coop netting incorporated with two layers of concrete—cement 1 part, rubble 2 parts. In section such ditches should be circular or oval and not V-shaped; the internal surface should be as smooth as possible. Grouted ditches must have key-walls about every 30 feet, while all cemented or plastered ditches must be perforated at 2-foot intervals with 'weep-holes' pointing upwards. In Europe and America many firms stock ready-made grouted drains in sections."[1]

"It is often feasible to regulate all the ditches of a locality by embanking and deepening them, or better by carrying away their perennial rain-water in drains, and adapting the ditches for the reception of storm water. If these ditches were paved, at least in some parts, the work would be more lasting and certainly very generally much more useful."[2] A single long ditch with permanent lining passing through a malarious, swampy area may be all that is necessary to convert an unhealthy into a healthy locality (Fig. 92).

One common cause of failure is the laying at too high a level of drains intended to carry off marsh waters or lower the subsoil water (Fig. 99). Another is the attempt to drain such waters into sewers or into storm-water surface drains. In many places brick drains have been laid where an open earth drain, or a subsoil tile drain laid deep enough, would have answered the purpose. Sometimes, again, extensive filling operations are undertaken where inexpensive subsoil tile drains are required.

Regulation of Surface Waters in India.—The chief surface waters here referred to are rivers, streams, irrigation canals, lakes, and natural and artificial collections of water of all kinds. Marshes are dealt with separately.

There are open to sanitary and irrigation engineers various systems of dealing with large surface waters. We will here deal with a few of the more important.

Regulation of rivers and streams.—This is an important factor in all general systems of prevention of malaria in India, and one of the most comprehensive ways of preventing inundations, which in endemic malarious districts give rise to the production of marshes and pools. The regulation of rivers and streams is dealt with *in extenso* in engineering works, and has an important bearing on the epidemiology and endemiology of malaria in India. The subject can only be briefly referred to here. Amongst the methods in operation are—vegetation on mountains and their slopes; steps, parapets and traverses; repellants or dams; rectifications and deviations and rough canalisation; regrading and training; settling or retaining basins; deviations and locks; embankments; works of defence against washing away of the bed; systematisation of the mouth, *i.e.* weirs or locks, or dykes in the sea.

Woods on the slopes of mountains.—These retain a certain proportion of the rainfall and yield it to streams by slow degrees. Deforested mountains, at every heavy fall of rain, permit of torrents descending from the slopes, which may cause excessive inundations of the plains.

Steps and parapets.—Steps and parapets on the slopes of mountains and hills materially lessen the velocity of the fall of water, and, when the slope is very precipitous, their construction is one of the few ways in which overflow of streams below can be prevented.

Traverses.—In the case of *torrential streams* and *rivulets*, by placing

[1] ALAN PARSONS in BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics*, Vol. II, p. 1661.

[2] CELLI, *Malaria*, p. 193.

obstructions of various kinds in their course, the force of the flow is much lessened. *Traverses* have been used for this purpose for centuries. They are usually in the form of trunks and branches of trees, large stones or any other available form of obstruction. They lessen the force of the current and reduce the amount of débris carried down. *Repellants* or *dams* operate in a similar way.

Rough canalisation of rivers, streams, etc.—By *rough canalisation* is meant the collecting of stones or mud on each side of streams, ditches, discharge canals, and water channels generally, so as to confine the water channels within the two sides of a limited surface, or deepening the beds here and there when necessary to remove marginal pools and give a straight and constant flow of water. This consists chiefly of rough canalisation of pools that are left by the contracting river after the monsoons, filling up small hollows, brushing larvæ over on to the sands, keeping free of grass and weeds any larger pools which cannot be drained, and the main channel of the river itself—all within half a mile above and below the town or cantonments concerned. Such work should be commenced each year at the end of the rainy season. Work of this kind in the lower parts of the streams may, of course, be carried away during flood times. Rough canalisation of rivers and water-courses generally has a wide application in the removal of breeding-places of anophelines in India. It is work that can be readily carried out if the right class of men, *malis* and agricultural labourers, is employed.

This may appear at first sight an enormous undertaking. In reality it is not so; in all cases mosquito gangs are practically sufficient to carry out the work. The writer is quite confident that such measures carried out in connexion with Indian rivers near towns, stations and cantonments would reduce the anopheline population in those places. In the case of all the larger rivers the work has to be continuous from the time these commence contracting until the flood time of the ensuing year. The number of men required will rapidly lessen as the river dwindles until a few are capable of doing all that is necessary. After heavy rains the work will often be laborious. Were the beds of Indian rivers properly canalised, embanked and kept within definite limits in towns and cantonments, as they are in Europe, all this would be unnecessary.

Regrading and training.—When the above fail, and an efficient flow is not maintained, it may be necessary to regrade the whole bed and train the banks.

Settling basins and locks.—These are used during flood times; they operate by allowing the water to flow into reservoirs in such a way that the overflow of the banks of the river is prevented (Celli).

Paving of beds of rivers.—*Paving* as a means of preventing the beds of rivers from being washed away has been carried out successfully in a few places. It is employed in some of the larger irrigation canal works in India, and it is a method applicable to a large number of streams which dry up during the hot weather but form large pools during and after the rains.

In the case of small streams the task usually resolves itself into renovating the bed and banks so as to remove the possibility of pools forming. In rivers, also, the banks should be seen to, so that side pools cannot arise.

Embankments.—To prevent inundation by rivers *embankments* are sometimes constructed, but even these may be overtopped and the whole of the neighbouring country more or less submerged. There are in India a large number of small rivers and streams near towns and cantonments that overflow their banks every year and leave anopheline breeding-places which last through-

out the malarial season. A certain amount of embanking would remove this very widespread source of breeding-places. The writer could refer to several stations where complete canalisation of streams would effectually remove all breeding-places. The same holds good, with some modifications, in regard to the larger rivers, such as the Ganges, Jumna, Beas, Ravee, Kistna, Godaveri and Brahmaputra, which after overflowing leave extensive breeding-places.

"A stream should be made to have steep banks directly above and below the flow line, uniform grade and width and a straight course, and be free from grass, sticks, stones and other obstructions that would interfere with the current. These conditions are seldom found in nature, but the nearer a stream approaches them, the less will mosquito-breeding be found."[1]

Streams and rivers which partly dry up, leaving depressions or holes created by the emptying of soft bottoms and forming pools in the bed along their course, are dealt with by filling in with stones (obtained from the bed) in such a way as to prevent further excavation by torrential waters.

Re-channelling of streams.—In cases where streams are very crooked and winding, and where much regrading is called for, it will often be better to disregard the old channel and construct a new and straight one. In wet and water-logged soil this is best done by blasting. Where the old channel is not specially crooked it will be much less expensive to utilise parts of it, straightening and regrading it where necessary, as shown in Fig. 93.

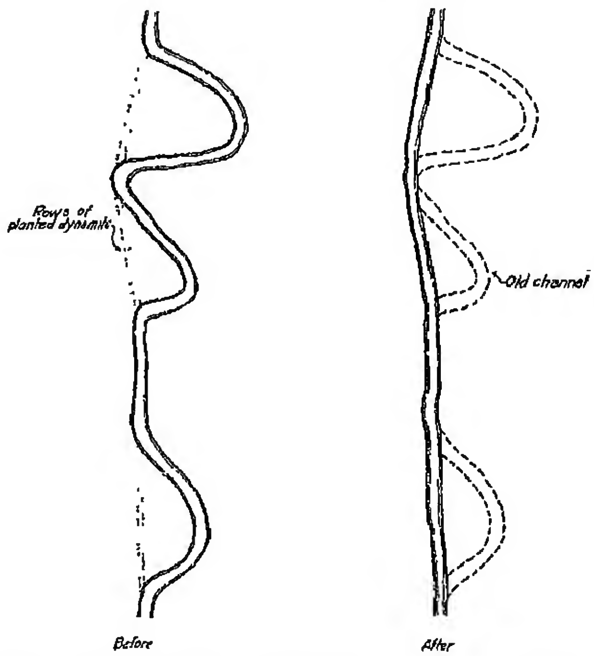

FIG. 93.—Stream before and after straightening by blasting.

Hill streams.—"Streamlets on slopes and hillsides, especially when among rocks and large stones, are often dangerous breeding-places. They should be trained and carried in a smooth plastered channel. Much excellent work of this kind has been done in Hong-Kong."

Disadvantage of unrevetted water-courses.—It may be here remarked that it is not possible to keep up an exact and uniform gradient in an unrevetted water-course, and that the *katcha* water channels of most Indian stations, by favouring the formation of pools, create many breeding-places for anophelines.

Carrying streamlets underground.—Subsoil drainage by tile pipes has sometimes been recommended for dealing with streamlets, but quite wrongly.

[1] LE PRINCE, *Malaria Control: Drainage as an Anti-Malaria Measure*, U.S. Public Health Service, Reports, 1915.

If it is necessary to carry a streamlet underground, it will often be found that this is best done in properly constructed iron drain-pipes with manholes.

Attention to small water channels.—Water channels require regular clearing of grass and weeds, and, when *katcha*, regular grading and levelling. The best-laid drain, in places where the fall is small, will, after a few months, if not regularly kept clear of silt, grass and weeds, become choked with sediment and vegetation. A simple clearing during the anopheline season is not sufficient; it should be carried out every fortnight, or at least once a month; the more frequently, the less labour each time.

Drainage of ravines.—Nothing can successfully replace subsoil drainage in ravines where the soil is sandy. A vast amount of money is wasted in laying down brick or concrete drains in such places. What happens is that the torrential rains of the monsoons wash away the soil at the sides of these drains, and finally the drain is isolated, much of the water it is intended to carry flowing outside it. Sand from the upper part of the ravine is deposited in the lower part, and ultimately more or less covers the drain. These disappointments can be prevented by laying down initially a complete system of subsoil drains. They should be at least 3 feet below the surface level, and should seldom be less than 6 inches in diameter. "In a narrow ravine a single line of pipes at each side of the hill foot intercepts all springs, and is often sufficient to dry the whole ravine completely. In wider ravines several lines of pipes are placed. The bottom of the ravine should be made level, so as to distribute storm water and prevent it cutting channels. If these form they should at once be filled in. In the steeper portions of the ravine, grass may be planted or turf pegged down, but this is not necessary as a rule. There being no water permanently on the surface, and no narrow channel, storm water produces a minimum of erosion. Silt coming from the hillsides is deposited within a few yards of the hill foot on the floor of the ravine, and is never carried down the ravine, as is the case in open drainage systems. The floor of the ravine becomes an absorbent pad through which water rapidly passes to the subsoil pipes, but which detains even the finest sand. The capacity of the pipes should be sufficient to dry the ravine completely in a few hours, even in the wettest weather. If the pipes are too small, drying is delayed, and one or more additional lines of pipes are called for. In laying them, a beginning is made at the head of the ravine. Where soil is required to level off the bottom of the ravine, it should never be taken from the lower edge of the hillside, lest springs be exposed. The cost of the system depends largely on the price of local labour. Ordinary agricultural tile pipes, which can be made wherever tiles are manufactured, serve the purpose best."[1] It has been found that the upkeep of this system of subsoil drainage costs roughly 5 per cent. of the capital cost per annum.

Brick and concrete drains.—These are seldom laid, except in towns, military cantonments and civil stations. In towns they are necessary on account of the foul liquids reaching them; ditch drains holding putrefying waste water soon become open cesspits and a dangerous source of disease. When brick drains are laid they must be self-cleansing; a drain 12 inches in diameter should have a fall of 1 in 100; in larger drains the fall may be less. In towns it is extremely difficult, if not impossible, to combine the sewage system with effective soil drainage; at any rate, up to the present, no satisfactory method of doing so has been devised, although this combination is most desirable in anti-malarial work.

[1] Sir Malcolm Watson in Byam and Archibald's *Practice of Medicine in the Tropics*, Vol. I, p. 258.

It is of the greatest importance that a suitable outlet for the main be provided in all cases, in order to prevent caving and possible closing of the pipe. A good protection is a concrete wall, in which the pipe is set (Fig 95, p. 345). "Where the outlet is low and liable to be submerged in time of flood, a valve should be installed to keep the water from backing into the drain." [1]

In laying a tile-drainage system, it is a good rule to lay only a few mains, connecting them with as many long laterals as may be necessary. No tile less than 3 inches in diameter should be used; in many agricultural regions nothing below 5 inches is employed. No fixed rule can be laid down. Many silt-loams of 40 to 50 acres are satisfactorily dealt with by means of 8-inch tiles and a fall of 2 inches in 100 feet, while in the same soil a 4-inch tile will drain only 6 acres. On level land with heavy rainfall the area that can be drained with these sizes of tiles is less by 25 per cent.

In laying the tiles begin at the outlet. They should be laid daily as far as the ditch is made. Delay in laying them may lead to injury to the ditch by rain or part of the walls falling into it. If the banks are likely to cave, the tiles must be laid as fast as the ditch is completed. Where a lateral joins a main or sub-main the connexion should be made with a Y. Neither a T nor an "elbow" is desirable, for obvious reasons. In sandy soil the sand may enter the joints and block the tile; this is prevented by covering the joints with strips of woven straw or old gunny. After the tiles are primed they may remain for several days without injury, until all the ditches are ready for filling. "If the soil is close and it is desirable to aid the water in reaching the tile quickly, the ditch can be partially filled with straw or brush, or better still with stones and pieces of brick. In laying tiles for intercepting seepage water, stone or gravel is much better than earth." [2]

Circumvallatory drains.—In the case of large marshes *circumvallatory* or *intercepting* drains are preferable to cutting channels through or across them—they are cheaper and usually more effective; in some cases, however, cross-channels are indispensable.

The ordinary way of drying damp soil, such as a swamp or marsh, is to dig a ditch around it or along its sides. Suppose we have a few acres of such soil to drain. The ground water will not be at the same level throughout this patch; it will be highest near the centre and lowest next the drain (Fig. 81, I and II). It is only when the level of the water in the centre is still too high for the purpose intended, whether mosquito control or agriculture, that a drain is cut through the centre. In properly drained land the water moves towards the drain as shown by the arrows in Fig. 81, I, p. 334. The farther the water has to flow in order to reach the drain, the greater is the friction, the slower is it in getting away, and the longer the water table remains high. If it is necessary to lower the water level still more the drains may be deepened; but in a stiff clay soil this may lead to the land next the drain being over-dry and the centre of the block still very wet. In that case another drain may be cut through the centre.

The importance of placing all culverts low enough to drain all possible mosquito-producing areas near by, and the abolition of all roadside borrow-pits, is well shown in Fig. 99, overleaf.

Rubble drains.—These are useful for lowering the level of the subsoil water. A channel of requisite depth, cut through or around a marsh, is filled with stones—large stones at the bottom, smaller ones on top. They are identical in principle with the subsoil drains used in certain parts of Ireland and of the

[1] Hardenburg, *Mosquito Eradication*, p. 128.

[2] "Tile Drainage on the Farm," *Farmer's Bulletin*, No. 524, 1917, U.S. Dept. of Agriculture, quoted in Hardenburg's *Mosquito Eradication*, p. 130.

continent of Europe. When water percolates through the interstices of the stones it carries away silt automatically and prevents the growth of grass and weeds. In certain localities these form excellent drains. Broken stones, clinker and pebbles are very useful for this purpose. In the Roman Campagna tufa in large blocks is used. These blocks are placed one along each side and another on the top so as to enclose a triangular space in the trench, which acts as a drain. Large pebbles may also be thrown into the bottom of the drain so formed.[1] By such a system of drainage, or some modification of it, extensive areas may be successfully kept dry; indeed, there are vast tracts in the Fens of Lincolnshire, in France, and in Germany that have been rendered healthy and non-malarious in this way. Such a system of subsoil drainage is largely applicable in certain towns, stations and districts in India where there is a high subsoil-water level.

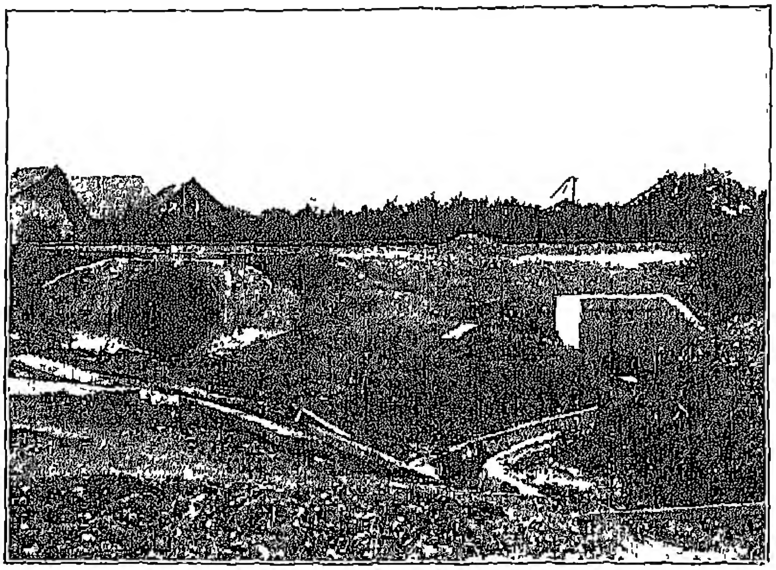

FIG. 99.—Culvert at Port Swettenham The photograph shows the old culvert on the left. The small culvert on the right is the low-level culvert put in by Mr Byrne. It is 3 feet lower than the old culvert, and has enormously improved the drainage of the town. The high tide of October, 1909, came over the railway at this point

From Sir MALCOLM WATSON'S *Prevention of Malaria in the Federated Malay States*, 2nd Ed.

Drainage by exhaustion.—"Extensive works have been carried out during late years for the drainage of large marshes in Italy such as those of Ostia and Maccarese. For this *hydrovorous machines* were used. The idea of this drainage, which is also called *drainage by exhaustion*, is very simple and ingenious. It is employed for marshes whose bottom is in some parts below the level of the sea, consequently it is not possible to cut ordinary discharging canals, there being absolutely no fall for the water."[2]

Accordingly canals are so cut as to intercept all water which can be discharged by gravity into the sea through an ancient *emissarium*. That which cannot is lifted by the hydrovores to a level which enables it to reach the *emissarium*.

Covering marshes with alluvium.—This fundamentally consists of covering lowland with soil. A river near at hand is allowed to flow over malarious land, and there deposits a considerable amount of mud, and thus,

[1] CELLI, *Malaria*, p. 163. [2] *Ibid.*, p. 201.

by utilising periods of flood, an area is gradually covered with a stratum of rich mould which has been washed down from higher land. This ingenious method has reclaimed various malarious marshes in Italy. MARSH writes —"The success with which human guidance has made the operations of nature herself available for the restorations of her disturbed harmonies in the Val di Chiana and the Tuscan Maremma is among the noblest, if not the most brilliant, achievements of modern engineering, and regarded in all its bearings, it is, as an example, of more importance to the general interests of humanity than the proudest work of internal improvement that mechanical means have yet constructed. The operations in the Val di Chiana have consisted chiefly in so regulating the flow of the surface waters into and through it, as to compel them to deposit their sedimentary matter at the will of the engineers, and thereby to raise grounds rendered insalubrious and unfit for agricultural use by stagnating water; the improvements in the Maremma have embraced both this method of elevating the level of the soil, and the prevention of the mixture of salt water with fresh in the coast marshes and shallow bays, which is a very active cause of the development of malarious influences." The method is to some extent applicable to certain districts in India, such as parts of the valleys of the Indus, Jumna, Ganges, Brahmaputra, etc. This system of natural covering has been extensively employed. It takes long, sometimes centuries, but the results are positive and satisfactory While this natural covering process is going on, the injurious effects it produces have been, and are, complained of. A typical instance in which this method is applicable is the *bela* land below the Fort and Daryaganj Cantonment in Delhi, but it would take many years to accomplish, and in the meanwhile malaria would be continuous (Fig. 45, p. 132).

Submersion or flooding.—It is a curious but well-known fact that whilst marshes are completely submerged they may be non-malarious. In suitable places flooding may render a swampy, malarious locality almost free from malaria. Instances of marshy places known to be excessively malarious having become more or less suddenly healthy are very common, the only change being that the marsh has become flooded with water, either naturally or artificially. If a stratum of water is made to cover a malarious site, so long as the water remains at a constant level there will be brought about a relative improvement. There are some historical instances of flooding having been resorted to during severe epidemic malaria with successful results. Submersion, however, is only comparatively beneficial. When other methods are economically feasible, submersion is to be avoided. The conversion of a malarious tract, such as a swamp, into a lake is a sort of paradox in the light of our present-day views of malaria.

In 1911 the west part of Maymyo (Burma, 3,900 feet) was decidedly malarious. It was more or less swampy in all its lower levels. The writer advised the creation of a lake into which the swamps at the west end of the station should be drained, and that 30 per cent. of the pine trees around should be felled. These measures were most successful.

The complete and permanent *immersion of marshes* as a means of converting an unhealthy into a healthy area has been known since the time of the ancient Greeks. EMPEDOCLES flooded the lowlands surrounding Selinos and thereby made this pestilential city healthy. In the last few centuries we have other instances in which this operation of simple flushing has eradicated malaria from whole districts in Western Europe. Dr. C. A. BENTLEY [1] tells us that there are certain parts of Deltaic and Eastern Bengal where flushing appears to be the only means of making any serious impression on the malaria.

[1] *Report of the Director of Public Health*, Bengal, 1924, by Dr. C. A. BENTLEY.

Subsoil drainage of seepage water from hills and removal of the causation of ponds, lakes and swamps.—Another method may be employed where *springs at the foot of hills* give rise to marshes and maintain a high ground-water level. Rain-water collecting between the surface soil and the underlying rock descends towards the bottom of hills, and increases the size of springs, which, collecting in hollows, form marshes. For these a circular trench which intercepts the water is made round the base of the hills. Other trenches then carry the water into larger ones, until they finally discharge into a stream or a river. When there are a number of springs it is advisable to endeavour to connect them and form one large spring, otherwise they form several small pools of water, which are specially prized by anophelines as breeding-places. The rate of flow in bodies of moving water has an important influence on the breeding of mosquitoes. CELLI has shown that a velocity of 63 mm. per second is compatible with the presence of larvæ of anophelines. Anophelines will be found to breed especially in sluggish running streamlets or rain-water runnels, in stagnant terrestrial waters, amongst weeds and grass in pits or holes in the ground, in hollowed-out rocks, in ponds and cisterns, but not in rapidly running rivers and streams.

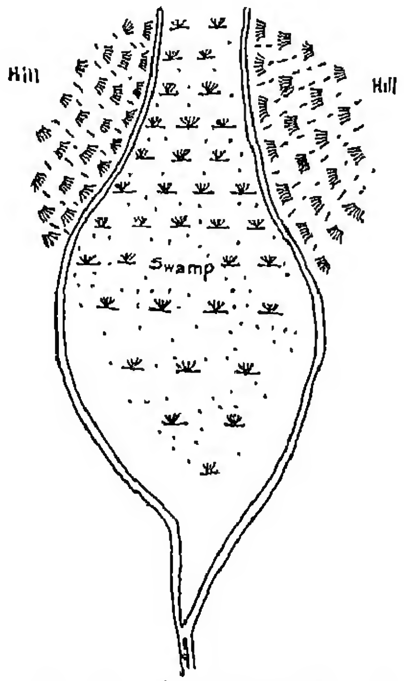

FIG. 100.—Seepage outcrop, case No. 1. (After METZ.) There was a seepage on both sides of a narrow valley, the water coming out of two hills opposite one another. A deep, narrow ditch was dug along the margin of each hill, just at the upper edge of the seepage outcrop and at right angles to the flow of the seepage water. The swamp, no longer fed from the hillside, has dried up.

From HARDENBURG'S *Mosquito Eradication.*

It is when we come to ponds, lakes and swamps, and seepage from hills, that the real problems arise, and it is best, perhaps, to consider these together. Since the difference between lakes and ponds is only one of degree, and since swamps may include either or both of these, it is obvious that, in actual practice, little distinction can be made that would involve different methods of drainage. It is more important to classify such areas according to the sources of the water, for in this case the distinctions correspond with modes of treatment. For instance, one pond or swamp may be caused by the accumulation of rain-water, and may fluctuate greatly with the seasons; another may be simply a basin in the channel of a sluggish stream; while a third may be fed from springs and may be bordered by a seepage outcrop. In the first of these, *the rain-water swamp*, it is merely necessary to provide a small channel to carry off the surplus water left after the main flood waters have passed. As a rule, one or two ditches will suffice.[1] There are thousands of rain-water swamps of this class in India.

"In the second case, *a basin in the channel of a sluggish stream*, the situation is more difficult, for the water supply is continuous and fluctuating. The swamp

[1] METZ, *Some Aspects of Malaria Control through Mosquito Eradication*, U.S. Public Health Service, Reports, 1919.

will vary in size with high and low water in the stream, and a drainage operation of considerable magnitude may be required to eliminate it. . . . In case drainage is decided upon, it will probably take the form of channelling the stream below the swamp to lower the water and increase the flow. The third case mentioned, that of a *swamp fed by a seepage outcrop*, presents the most difficult problem of all. Here we have, not only an area of standing water, probably full of vegetation, but also a series of tiny puddles in the form of hoof-prints, etc., along the outcrop margin. Each of these is a potential breeding-place of the worst kind. The treatment of such an area requires a special procedure, and since the proposition is one that is apt to be found in almost any locality, it may be considered in some detail.

"Seepage water usually appears on the hillsides, etc., at the outcrop of a stratum of water-bearing sand or gravel underlain by an impervious stratum of clay, shale or other material. The outcrop may be in the nature of more or less distinct springs, or simply a gradual oozing out through the soil. In either case it is fed by a water-table below the surface, and treatment must be aimed particularly at this water table. It does not suffice to dig ditches directly away from the springs and down the hillside. Such a method would require a separate ditch for each spot from which water is issuing, and would mean in many cases a series of ditches about 12 inches apart along the whole hillside. The only effectual way of collecting the water in such places is by means of ditches dug *at right angles to the flow of the seepage water*, or, in other words, across the exposed end of the water table. Such ditches may then be connected to one or more main ditches, if necessary, and the water carried down the hillside parallel to the seepage flow.

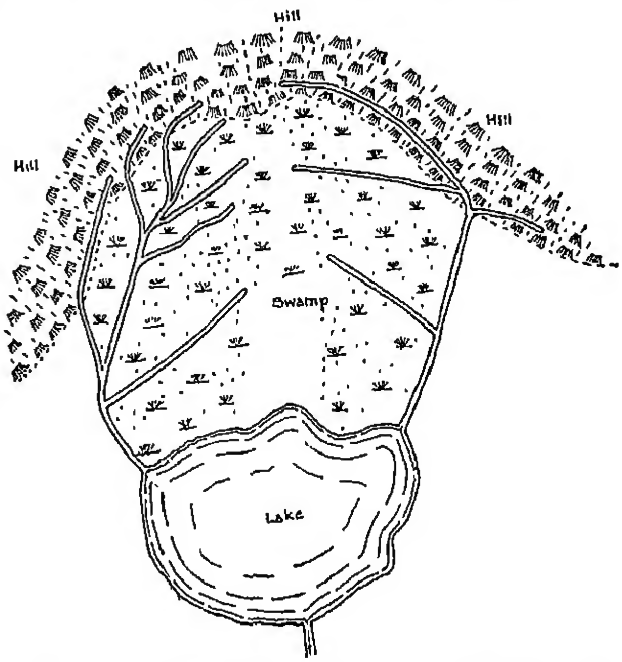

FIG. 101.—Seepage outcrop, case No. 2. (After METZ.) The seepage flow is from a large U-shaped bend in a hillside, resulting in a swamp many acres in extent, with a small lake at the outer edge.

From HARDENBURG'S *Mosquito Eradication.*

"In case No. 1 there was a seepage on both sides of a narrow valley, the water coming out of two hills opposite one another, as shown in the sketch. As a result the bottom of the valley in this region was a typical cat-tail swamp, with water from 1 inch to 2 feet in depth. Since the source was somewhere up the hillside, it was useless to dig a ditch through the bottom of the swamp and down the valley. This would simply carry off the deep water and leave the seepy marsh just as it was. Instead a deep, narrow ditch was dug along the margin of the hill, just at the upper edge of the seepage outcrop, and at right

angles to the flow of the seepage water. In this manner the water table was intercepted, and all the water that formerly oozed out down the hillside now seeps into the ditch and is carried off. As a result the swamp, no longer fed from the hillside, has dried up.

"In case No. 2 a more complicated situation is presented. Here the seepage flow is from a large U-shaped bend in the hillside, resulting in a swamp many acres in extent, with a small lake at the outer edge. The water table in this case extended clear across the swamp, but was concealed along a slight elevation running down the middle. On account of this elevation it was necessary to drain the right and left halves of the swampy area separately. As shown in the sketch, a ditch was put along the toe of the hill on each side at the upper margin of the outcrop and then run off into the lake. But the water table this time was too deep to be intercepted entirely by one ditch, and it was necessary to dig additional intercepting laterals at intervals lower down. On one side five such ditches, more or less parallel to one another and at right angles to the seepage flow, were required to catch all of the water before it came to the surface.

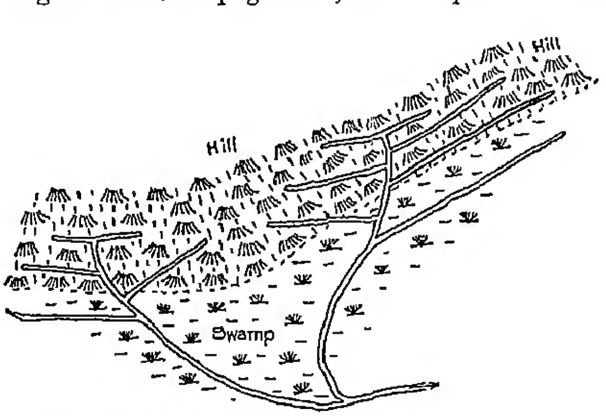

FIG. 102.—Seepage outcrop, case No. 3. Outcrop on a relatively steep hillside. (After METZ.)
From HARDENBURG's *Mosquito Eradication.*

"In case No. 3 an outcrop on a relatively steep hillside is represented. Here it was necessary to dig several intercepting laterals, parallel to one another and only a few feet apart, in order to catch all of the flow. When this was done over the area in which the seepage water was actually coming out of the ground, the remainder of the swamp lower down the hillside became completely dry.

"In each of these cases collection of water depended upon the ditches being constructed primarily as intercepting rather than conducting ditches. In the case of swamp No. 1 the ditches happened to be intercepting and conducting at the same time; but more often separate conducting ditches must be constructed to carry off the water after it has collected in the intercepting ditches."

Vertical drainage—principle of.—It has long been known in agricultural districts in certain parts of Europe and the U.S.A. that vertical drainage is an effective and economical way of getting rid of ponds and large pools held up by an impervious stratum overlaying a pervious one. It has been practised in many countries. The principle is that of boring a hole through the impervious stratum so that the suspended water may escape through the porous layer beneath. This porous layer may be coarse or fine gravel, limestone, or other formations containing fissures and seams. The reverse operation is adopted in the sinking of tube wells, which are now being used as sources of public water supply in various parts of India, but in boring for water the depth of the boring has to be considerably greater. There is an element of uncertainty in vertical drainage, but as the expense where the pervious layer is close to the surface is slight as compared with costly ditching, it is well to make the

attempt in favourable districts where it is necessary to get rid of ponds, tanks and large pools. The holes should usually be lined (Fig. 103) to prevent blocking up of the escape passage for the water by erosion, and it is likewise desirable to construct a drain-head (Fig. 104, p. 356) or other device to keep out th coarser material carried by the water.

Vertical drainage for large areas.—Sometimes, when the area to be drained is extensive, it is necessary to make the hole of considerable size. This, of course, greatly increases the cost of the operation. STROMQUEST[1] describes such a hole which drained a pond covering more than 40 acres in extent. A shaft 7 feet square was sunk to a depth of about 41 feet, at which point a fissure, about 4½ feet high by 1½ feet wide, was found in a vertical wall of limestone. The shaft was curbed by 2″ × 6″ material, double braced at intervals of 3 feet, and 2″ × 12″ sheathing. A flume was built from one side of the shaft to the end of the ditch connecting with the lake. The outlet thus formed proved sufficient to drain the entire lake and keep it dry. Sometimes, if the fissure be small, there is a tendency for the hole to silt up, especially when the water enters the hole directly. This may be avoided by the use of a drain-head designed to keep out floating matter and the coarser sediment. This drain-head may be an elongated, narrow box, laid as a pipe from the ditch to the hole; the end towards the ditch should be heavily screened, and the other tightly closed; a hole in the bottom near the closed end, through which the water is to enter the shaft, also should be well screened; a door at the top of the box will allow this latter screen to be cleaned from time to time; the entrance screen, of course, may be kept clean from the outside.[2]

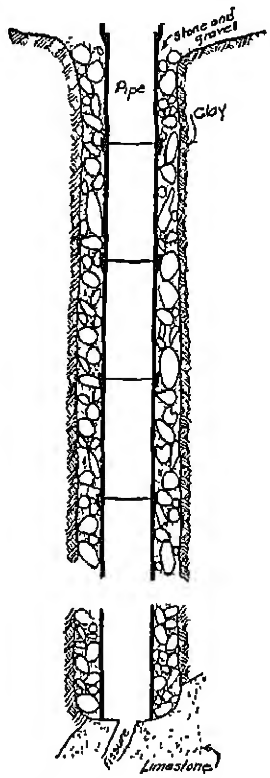

FIG. 103.—Sketch of vertical drain.

From HARDENBURG'S *Mosquito Eradication.*

Vertical drainage of large ponds, tanks and swamps may be successfully carried out by sinking shafts as described above. In many places it is necessary to pierce a clay stratum of from 30 to 50 feet or more before the gravel or porous stratum is reached. It is specially suitable for endemic malarious areas where a thin impermeable layer of soil rests upon a deep permeable one. This was suggested to the writer by watching for two years the various strata excavated in the sinking of tube wells in several towns and military cantonments in the Punjab. In 1919 the Chief Engineer, Northern Command, was about to sink these drainage shafts in the cantonments of Ambala, Lahore, Agra and other stations, where large ponds, tanks and marshes existed, but the work had to be abandoned on account of the outbreak of the Afghan War.

Conversion of marshes in or near towns into ornamental waters.—Failing other methods it may be advisable to convert marshes or swampy areas in the neighbourhood of towns into ornamental waters surrounded by stone or brick walls cemented inside.

Flushing.—In exceptional circumstances, where water is available, flushing of marshes may be a useful operation by carrying away larvæ. This is one of

[1] HARDENBURG'S *Mosquito Eradication*, pp. 133, 134. [2] *Ibid.*, pp. 133, 134.

the natural means of keeping down mosquito-breeding during the torrential showers of the monsoons.

Regulation of irrigation waters.—Successful irrigation depends as much on the effective disposal of the effluent as on the actual water supply to the crops. Defectively drained irrigated land is of less value agriculturally, and is liable to be more malarious, than irrigated land in which, by properly regulated effluent channels, the water in the soil is fully under control. In many instances the disposal of the effluent is left unthought of. This is an almost invariable rule with the irrigation carried on from wells by ryots and from many irrigation tanks, and even in some cases from irrigation canals. The result is a soil saturated with water.

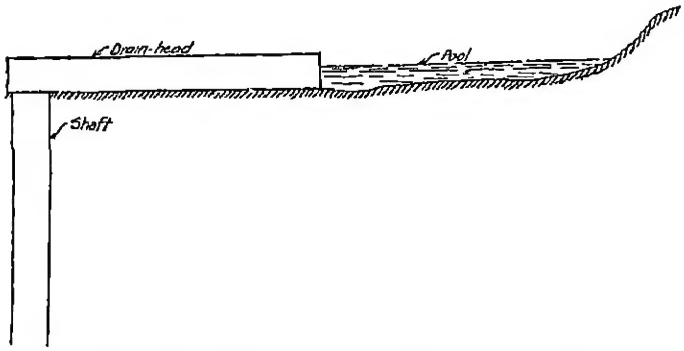

FIG. 104.—Profile of pool, drain-head and shaft. From HARDENBURG'S *Mosquito Eradication*.

This is one of the great causes of the prevalence of fevers in agricultural villages and on the outskirts of towns where rice is the main crop, for such villages are always adjacent to the fields themselves, the water table is high, and the existence of breeding-pools for anophelines is universal. It has been suggested that, if the water from irrigation channels can be kept flowing at a certain rate over the fields, mosquitoes would be prevented from breeding in them. Whether this would act efficiently or not could be readily put to the test in irrigated rice and sugar-cane fields. We should remember that the agriculturist's scheme to retain water is not always the best from an anti-malarial point of view. The solution of the ryot's problem is best worked out in the field with the combined skill of the malarial expert, the engineer, and the agriculturist himself.

Whenever irrigation works are carried out, or any other works which will increase the amount of water in the soil, it is necessary simultaneously to carry out adequate subsoil-water drainage, in order to remove the effluent. Neglect of this in India will invariably be associated with increased malarial endemicity in all newly irrigated districts.

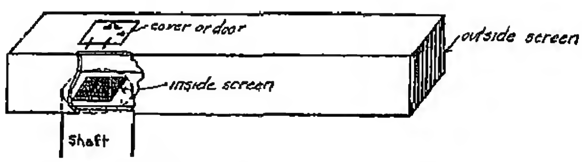

FIG. 105.—Sketch of a drain-head for vertical drainage. From HARDENBURG'S *Mosquito Eradication*.

Improvement in the method of control of the distribution of irrigation-channel water to crops is most important. As regards malaria one simple solution at once suggests itself—intermittency. How far this is compatible with the normal growth of crops is discussed below.

The beds of most irrigation canals in India are porous, and the subsoil water of the bordering land, and for a varying but often considerable distance beyond on both sides, is practically at the same height as the upper level of the water,

sometimes higher. This conduces to the formation of one of the most favourable breeding-places for Anopheles in the whole area affected by the water in the canals. The same state of affairs exists, but not to such a pronounced degree, in the areas through which the branch canals and supply channels run.

Use of some impermeable material for lining irrigation canals, channels and *katcha* drains.—One of the best methods of covering the sides and bottom of ordinary earth drains is that of lining them with a hard waterproof material consisting of asphalt and sand, which prevents the growth of all vegetation in the drains and is not scoured out by tropical rains. A mixture of liquid asphalt and sand heated to a high temperature, projected over the surface of a wide ditch and allowed to cool will form a hard asphalt-sand wearing surface. The details of this particular type of impermeable drain are not given as asphalt is not obtainable in India. The writer has introduced this type of drain lining here with the sole object of illustrating a principle, Like many sanitarians of India, he knows that the heavy leakage from irrigation canals and channels is responsible for an enormous amount of endemic malaria. A lining of this kind, or of something that would answer the same purpose, for irrigation canals and channels would solve one of the most difficult problems

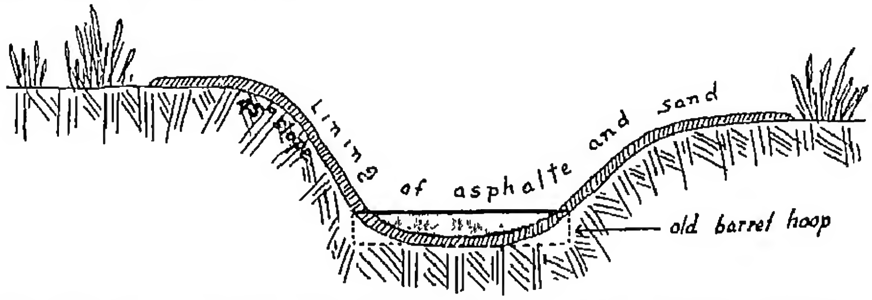

FIG. 106.—Cross-section of a ditch (*katcha*) drain lined with an impermeable layer of liquid asphalt and sand.

From *Trans. Roy. Soc. Trop Med. and Hyg.*, Vol. XVI, No. 3, June 22, 1922, p. 105; *Anopheles and Malaria Control*, by ERIC DE VERTEUIL, M.B., B.Sc. Lond.

the anti-malarial sanitarian has to deal with in irrigated lands—viz. the dangerously high subsoil-water level. Is it not possible for irrigation engineers to devise some way of doing this at a reasonable cost? The initial estimates in canal building would be higher, but the benefit to the people worth it.

J. A. S. PHILLIPS [1] gives a highly interesting account of the health of the towns of Saharunpur, Nagina, Kosi, Meerut and Lucknow before and after anti-larval measures were put into operation. In the year 1900 the late Colonel J. C. ROBERTSON, C.M.G., C.I.E., I.M.S., stated that well irrigation lowered the subsoil-water level, and, owing to the labour involved, rarely saturated the soil sufficiently to produce breeding-places, whereas canal irrigation raised the subsoil-water level to the extent that pools might form in depressions of the sodden soil. Canal irrigation and rice cultivation were forbidden in and near the town of Saharunpur (this prohibition was withdrawn in 1922), tanks and boggy land were filled, and drains and *nullahs* properly looked after. In 2,500 children examined on each occasion the percentage of palpable spleens fell from 78·8 per cent. in 1909 to 7·3 per cent. in 1923. In the same period the parasite index fell from 53·8 to 10·3. In like conditions the splenic and parasite indices fell in Nagina from 79·1 and 44·4 to 13·4 and 6, in Kosi from 81·3 and 26 to 42·5 and 6·3, in Meerut from 5·9 and 6 to 1·3 and 3, and in Lucknow from 2·2 and 7·4

[1] "On the Results of Anti-Malarial Measures in Five Towns in the United Provinces," *Ind. Med. Gaz.*, May and June, 1924.

to 1·6 and 0·1. The writer believes this to be one of the most remarkable records of anti-mosquito measures in Indian malarial literature, deserving serious consideration as regards the effects of irrigation.

Disposal of effluent from rice-fields.—Rice-fields and irrigated tracts of land as factors in malaria call for special consideration, as they are mostly connected with the artificial control of water. Rice-growing requires a large supply of water, the young plants being kept almost submerged for some weeks, but there should be in connexion with this an efficient system of effluent drains. The fields should be completely flooded; areas only partly covered with water are liable to contain Anopheles larvæ. Fully flooded fields are often found to contain small fishes. As a rule the amount of water coming into the fields is well under control, but the effluent drains (if there are any) do not work efficiently. If both are completely controlled a uniform level of water may be maintained, and when the water is no longer needed the afferent channels are closed, the water in the fields drains away, and the soil dries. Some authorities consider it desirable to devise, as an anti-mosquito measure, a means of keeping the irrigation water on the rice-fields moving slowly, say 10 to 12 yards a minute.

In the feeding channels and effluents, which should be kept free from grass and weeds, Anopheles larvæ are sometimes found. Breeding in them could be prevented by having two supply channels, using each alternately for a week, thus allowing one of them to dry each week; in the drying process all larvæ are killed. This is a very simple and cheap way of controlling this form of mosquito-breeding. It has been carried out by the brothers SERGENT in Algeria, who consider it to be very effective. They say that the success of this method in Algiers depends on the dry climate and the life-period of the larvæ there being three weeks.

As soon as the crop is ripe the efficiency of the effluent drains should be seen to, it being important that the whole of the fields should be uniformly dried as rapidly as possible.

The subject of the control of malaria in rice-growing districts in India and Burma is of the highest economic importance. Our knowledge is as yet far from complete, but it is sufficient to indicate the lines upon which further investigation should be made.

In some flat rice districts, especially those of Central Burma, the writer failed to find Anopheles larvæ in the rice-fields, although the adjacent swamps contained the larvæ of malaria-carriers. Rice-fields, then, are not necessarily associated with malaria. There are thousands of square miles under paddy cultivation in Southern India in which Anopheles do not breed. It has further been shown that, when they do, mosquito larvæ die rapidly in rice-fields that are drained temporarily. Expert agriculturists are now investigating this question more thoroughly to ascertain if any use can be made of this discovery. The operations being carried out, the writer understands, are draining the rice-fields twice a month, thus exposing larvæ to the direct rays of the sun, and observing the effect on mosquito production and on the crops.

It has been ascertained that the rice grounds in some parts, such as Trichinopoly, Tanjore, and other places in Southern India, where the plantations are almost constantly inundated,[1] produce less malaria than those which, after inundations, are exposed to the action of a powerful sun. This consideration will assist in explaining the different degrees of unhealthiness in the neighbourhood of the rice grounds in various parts of India.

[1] Because owing to an abundance of water they are able to raise three crops in the year. In rice cultivation under tanks the cultivation lasts from October to April, only two crops are raised, and the land lies fallow during the hottest months. In the districts named cultivation goes on for nearly the whole year without intermission, and the ground is always saturated with water.

As stated above, the diverse conditions found on the paddy fields of India are essentially those of marshes. Hence, if a site for habitations in a malarious locality must be selected in the neighbourhood of wet cultivation, surface drainage should be such that the "tail" of water beyond that requisite for plant life must be correctly disposed of.

As now carried out, "wet" cultivation is responsible for an enormous amount of malaria in India, Assam and Burma. It is possible by legislation to prevent such cultivation within a certain limit of densely inhabited towns, cantonments and civil stations as is done in Italy, but under the general conditions of agricultural life in India it is not possible to adopt this measure in rural malarial districts, where the small collections of huts called villages are in most districts scattered in the very heart of the rice-fields themselves. In endemic malarious districts it is theoretically justifiable to condemn rice cultivation, but in India, where millions depend on rice crops for their existence, this rigid attitude towards rice production cannot be adopted. It is often, in severely endemic malarial districts, a question of allowing the lower classes to die of famine or die of malarial disease.

Other forms of wet cultivation provided with irrigation water, such as sugarcane, can, without detriment to the plants or reduction of the crop, be fed with the water periodically, the surface being allowed to dry sufficiently to kill larvæ in the intervals between the irrigation. The writer, during many years' observation, only found *Anopheles* larvæ twice in flooded sugar-cane fields, once in Bijnour (1906) and once in Shahjehanpur (1909), both in the United Provinces.

Land springs.—Land springs creating marshes, as they are specially likely to do when several lie adjacent, may be collected into one or more underground drainage pipes in the manner already explained (pp. 352–354).

Ponds and tanks unconnected with marshes.—The rain falling on the catchment area of ponds and tanks produces runnels which fissure their perimeter. *Katcha* intercepting drains, cut as explained for marshes and discharging elsewhere as circumstances permit, will obviate these.

In towns and cantonments, when tanks are about to be filled in, some arrangement should be made in connexion with these *katcha* intercepting drains to allow refuse carts (when dry refuse is being used for filling) to reach the tanks—old spare iron pipes at the bottom and covered with earth will answer the purpose. When the tank is itself filled up, the intercepting drains should also be abolished before the work is finally quitted. A number of tanks and borrow-pits have shallow and deep parts; where the work of complete filling cannot be carried out, the shallower parts should be filled. This would give a smaller area of water surface for anophelines to breed in, the deeper parts being taken in hand when funds for the purpose can be spared. Deep waters are not favoured by anophelines. Regarding the vertical drainage of tanks and ponds see pp. 354, 355.

The general measures for dealing with large ponds and tanks include—clean banks free from vegetation, absence from the surface of the water of all floating débris and vegetation, if possible fluctuation of water level, a minimum area of shallow overflow during the rainy season, introduction of surface-feeding larvivorous fish, periodical inspection of the pond or tank. Besides this, particular ponds and tanks may call for other special measures, the nature of which can only be determined by close investigation.

F.—FILLING OPERATIONS, ETC.

These operations, though not altogether satisfactory, are important; sometimes as important as drainage. *Large* filling operations should never be adopted until the result of a complete series of levels has shown that the land cannot be properly drained; in most cases open-ditch drains should be tried

first, and afterwards deepened if necessary. Filling is always costly. It is legitimate when it is the cheapest way of obliterating small breeding-places, such as disused wells and similar depressions which expose the water table, and should be undertaken in the non-breeding season of Anopheles.

Filling in India is mostly done by manual labour, but in large operations it is more economical to use suction dredgers, steam shovels, or other kinds of machinery.

The filling in of swamps is often a waste of money. Sir MALCOLM WATSON says: "To fill in a swamp at a cost ten times what would be sufficient to drain it, means that nine other swamps remain undrained." But it may be that filling in will improve the land, rendering it cultivable and profitable, in which case it is justifiable. If filling in is resorted to, the natural outlet should be the last part to be dealt with, otherwise the swampy condition will be aggravated, and possibly an outbreak of malaria precipitated, or the endemic malaria already in existence intensified.

Dry refuse for filling tanks and borrow-pits.—There are many collections of water in and around towns, stations and cantonments which may, without risk to health, be filled up with dry refuse, provided they are not within 100 yards of villages or within 200 yards of bungalows and barracks. Stable refuse, so used, breeds flies unless special care be taken to render it uninhabitable to maggots. It should be kept dry and covered daily with earth. In all cases the final levelling should be carried out with a layer of earth several inches deep. When filling up large excavations with dry refuse is decided upon, the work should be carried out systematically, begun during the cold weather, and, where possible, completed before the ensuing rains. If the capacity of the excavation is too large to complete the filling and levelling before the rains, it should be divided up into sections by one or more *katcha bands* of mud walls, and each section taken in turn, the object being to prevent decomposition and fermentation through admixture with water. The earth for these *bands* may, if there is no rising ground in the neighbourhood, be taken from the margin of the excavation.

The shallower parts should be taken in hand first. If the deeper parts contain water, this should be baled or pumped out before the filling is begun. In places where there is little or no earth and draining is impossible, this is the only way available without inordinate cost.

Small ponds, pools, and collections of water that cannot be otherwise dealt with, should be filled in. Wet areas, which are the most difficult to deal with, should be taken in hand first.

Most deep tanks with steep, clean edges do not harbour Anopheles larvæ. If they shoal and deteriorate they do, and require attention.

Lowering the level of the general surface for filling excavations.—In many instances depressions may be filled up by removing uniformly several inches of earth from the surrounding area. On the plains the soil is often a sandy alluvium and moderately porous, so that a superficial reduction of the level is not likely to lay bare the water table. Strict supervision is, however, necessary to ensure that such lowering is quite uniform and that no pits or irregularities of the surface are created.

The filling in of borrow-pits.—Any neglect in connexion with the filling up of excavations and borrow-pits caused by building operations is dangerous—these should at least be drained before being finally quitted by workmen.

No rule can be laid down for borrow-pits; they should be dealt with accord-

ing to the conditions found. A very large percentage of borrow-pits, especially freshly made ones, do not breed mosquito larvæ at all; a vast number of borrow-pits breed only culicines and *A. subpictus*; it is *only those containing malaria-bearing Anopheles that call for action.* Further, no one would think of dealing with borrow-pits breeding Anopheles miles away from human dwellings. Those that have to be dealt with may be shallow, small, and, in relation to the drainage of the land, so favourably placed that simple cutting or ditching is all that is called for. But they may be large and too deep for anything except vertical drainage (p. 354) or being stocked with fish; even for many of these an outlet ditch may often be made successfully; anyhow the possibility of ditching should not be left unconsidered.

With a view to decreasing borrow-pits as a source of anophelines it has been suggested that material for road-making be taken about 20 feet from the edge of the proposed roadway, which gives a wide berm. The draining of borrow-pits is said to be objectionable from an engineering point of view as running water tends to scour out the foundations of the roads. There is little to support such a view. The object of such drainage is to do away with borrow-pits and their consequent collections of stagnant water; it has nothing to do with the general drainage of the neighbouring country. With such drains the borrow-pits would dry up and cease to be what they are now, nurseries for mosquitoes. A small, properly graded drain along the side of roads is sufficient for the drainage of the road itself. The remedy for roadside borrow-pits appears to lie in the construction of graded *katcha* drains in all the borrow-pits now in existence at the sides of roads. These should have an oval bottom, and be about 1 foot in diameter and 9 inches deep. Such a system would remove the present risks. It would be more economical than grading the whole of the borrow-pits and cheaper in the upkeep.

Creating borrow-pits to be strictly interdicted.—It is essentially necessary that the excavation of earth for building purposes or other works should be rigidly prevented within half a mile of towns, cantonments and civil stations, and 200 yards of villages. There will be great difficulty in giving effect to this recommendation, and it is doubtful whether compulsory legislation regarding it would be passed. In the later years of the writer's administrative career, with the help of the Chief Engineer of the Northern Command, this rule, as regards cantonments, was consistently observed. Legislators should remember that practically all the tanks and ponds in and around towns and cantonments, and the ponds of villages, began as small borrow-pits, created by removal of earth for building. To sum up, the construction of houses, barracks, etc., should not be considered complete until every excavation created has been filled up and properly levelled. Slight depressions of the general surface, irregularities in surface drains, shallow pits and hollows, which lodge water only for a short time after the rains, should all be abolished, as they serve as breeding-places for at least a few generations of anophelines. It is important that these generations be prevented, as the thousands they give rise to at the beginning become millions during the latter part of the breeding season. Incidentally, it might be said that water in freshly made borrow-pits is not selected by anophelines, but after the pits have been in existence some time, and vegetation has grown in and around them, they become breeding-places, especially along roads provided with umbrageous trees giving shelter from the direct rays of the sun, and in the neighbourhood of human habitations.

Many engineers look upon the creation of borrow-pits as inevitable in the making of roads and railway embankments as the earth required has to be got from somewhere close at hand. If this is accepted, then pits in water-logged areas should be large and deep, so that they do not dry up and kill fish,

and they should not be allowed to become swampy and full of weeds when situated within half a mile of human habitations.

Emptying small ponds and pools with portable pumps.—For comparatively small ponds and pools of water, especially borrow-pits, one of the most immediate and direct ways of getting rid of water is by using a *portable pump*. Merewether's pump is considered the most satisfactory for the purpose. The water is pumped into a natural water-course or drain, if there is one at hand, or over a wide area to be absorbed and evaporated. This is a most useful accessory method, but at best only a temporary expedient. An ordinary hand-pump may also be used in this way. The writer has used this method extensively for small collections of water in cantonments; a few men of a mosquito gang can empty the water from many small ponds and pools in a week in this way.

Tanks, ponds, pools and borrow-pits that cannot be drained or emptied, if they are found to be breeding anophelines, should be kept free from aquatic vegetation, their banks made perpendicular, and the larger of them stocked with larvivorous fish.

Ornamental ponds.—Many permanent collections of water breeding malaria-carrying Anopheles may, if in suitable places, be converted into ornamental ponds, or even bathing pools, by surrounding them with a low stone, brick or concrete parapet with cement or concrete sloping down into the circumference of the pond for a few feet. It is rare to find anopheline larvæ in ponds or tanks treated in this way.

Pools and puddles.—These, being always present and being the sites favoured by Anopheles for oviposition, are most important. Filling is the most permanent and cheapest way of obliterating them. They may also be drained, often by the removal of a spadeful or two of earth.

Disused wells.—Disused wells swarm with culicines, and occasionally *A. stephensi* breeds in them prolifically. They should be filled in or adequately covered or screened.

Brick factories.—The borrow-pits of brick factories form breeding-places for anophelines during, and for a few months after, the rainy season. No brick factory should exist within 1,000 yards of municipal or cantonment limits, and in selecting sites for brick-kilns, even at this distance, the possibility of future extension of these boundaries in the direction of the site chosen should be borne in mind. The building of houses and huts with *pukka* bricks made on selected sites, instead of sun-burnt ones made on the spot, would to a large extent do away with the creation of borrow-pits and tanks.

Grass farms.—No land within 400 yards of municipal or cantonment limits should be used for grass farms when, within 100 yards of the grass land, there are collections of water known to be breeding-grounds of anophelines. The grass in the latter case, even when half-grown, affords abundant rest and shelter to anophelines when passing from these breeding-grounds to feed on man, and again when returning to lay their eggs.

Mosquito brigades.—These are organisations for dealing chiefly with collections of surface water, but may be used in many ways for reducing mosquitoes, adult and larval. They were first suggested and created by Sir Ronald Ross. In practically all the operations needed for the removal of the smaller breeding-grounds of anophelines, and for the destruction of larvæ in small collections of water, mosquito brigades are usually sufficient. The work of mosquito brigades is applicable to a great variety of places in India—towns, collections of villages, cantonments, jails, and all large industrial works and factories; the writer would emphasise the necessity of their employment wherever

large gangs of labourers are employed on famine relief works, making of railway embankments, roads, canal works, tea gardens, extensive building operations, etc. In these latter cases half a dozen of the coolies under one headman could be taught their duties in a few days. A few gangs of such men working efficiently can prevent much of the malaria in aggregations of labourers. The same remark applies to troops who are obliged to encamp in an endemic malarial district *en route* to or from campaigns—a few soldiers placed on special sanitary duty may prevent hundreds of cases of malarial infection. The duties of mosquito brigades are given on p. 373.

The writer concludes this section with some sound advice given by Sir Ronald Ross: "Attack first those collections of water the obliteration of which will remove the largest number of mosquitoes for the least amount of money. Thus it is quite useless to drain stagnant water because it is stagnant. The superintendent (of the mosquito brigade) should first assure himself that it does actually contain larvæ, and better, that it constantly contains them. Some pools are too large, others too small, and others are subject to scouring, and though these conditions often change at certain seasons, when, for instance, large pools dry up, yet some pools appear to be habitually unsuited to mosquito larvæ. It is useless to spend much money over these. Again, it is not advisable to attack without discrimination even the pools which do contain larvæ. Some contain many more larvæ than others do, and in my experience, while larvæ do occur in some considerable bodies of water, such as marshes or large pools, they are generally much more numerous in small pools. Now it is evidently bad economy to spend large sums over draining large bodies of water when small puddles, easily dealt with, really cause the mischief. The superintendent must *suppose* nothing—he must never suppose because a marsh exists in a neighbourhood, that it is the only or principal cause of malaria. He must study the point by careful search for anopheline larvæ, and may often find that a small unobserved pool in the street is more dangerous than a marsh a mile away.

"The number and nature of the breeding pools depend so much upon the configuration of the ground, the character of the soil, and the amount of rainfall, that it is impossible to give minute directions regarding the method of dealing with them. The superintendent must be guided by his own judgment, remembering only the maxim which applies to most kinds of work, *adopt the smallest measures first.*"

Of the simpler anti-mosquito measures the most comprehensive in its effects, and the most generally useful, is that of doing away with all stagnant collections of water in the neighbourhood of private dwellings, villages, towns, civil stations and cantonments, by filling up hollows and irregularities, or by draining them.

G.—CULTIVATION AND ARBORICULTURE AS ANTI-MOSQUITO MEASURES

Cultivation of the soil.—Until the discovery of the malaria-mosquito relationship there was, apart from the use of quinine, practically only one method of general prevention of malaria in operation in rural districts amongst civilised nations, that of *cultivation* of the soil, in which was included the *regulation of the level of the ground water*. The latter is dealt with on pp. 333–337. Drainage and cultivation are specially applicable to areas where these can be carried out profitably. Complete and permanent drainage of

malarious land that will not repay the cost of draining and cultivating cannot be recommended, but when agricultural development goes hand in hand with the drainage of swamps and marsh lands the cost is soon defrayed.

In a general way it would appear that the existence of proper cultivation of the ground and malaria have from the earliest times been antagonistic to one another; in regions where cultivation has been neglected malaria has prevailed, and when husbandry has been systematically carried out in malarious places, there malarial diseases have greatly decreased or completely disappeared. In general terms it may be stated that all the more approved methods that have been employed on a large scale, and that have stood the test of time, have had the common object of regulating the level of the ground water in such a way as to enhance the fertility of the soil. "History teaches that if man has frequently sacrificed himself for the redemption of unhealthy places, it is nevertheless true that unhealthy lands can only be cultivated at the risk of the life of the workmen and the substance of the owner" (CELLI).

Many parts of the world formerly highly malarious have become, by means of intensive cultivation and arboriculture, converted into exceedingly prosperous and salubrious places, *e.g.* parts of Northern Italy, and many of the countries in the Southern and Central U.S.A. Algeria is now an admirably cultivated and prosperous region without malaria, although years ago it was a hotbed of severe malaria; by clearing and intensive cultivation it has become a veritable health resort. The anti-malarial value of intensive culture lies in the resulting increased prosperity with its improved quality and quantity of food, clothing, better housing, and medical care. Intensive agricultural development has much good in store for India if it is adopted.

Levelling and ploughing.—*Levelling* and *ploughing*, etc., of land under cultivation have some effect in reducing malaria by making the soil more permeable to water and preventing the formation of pools.

Intensive cultivation.—*Intensive cultivation*, which is best represented by the rapid rotation of crops in market gardens, has rendered many areas less malarious and in some cases has quite eradicated malaria. It is also profitable where it can be brought into operation. Land which has been under cultivation, when long neglected, becomes a focus of endemic malaria. This is the origin of part of the malaria in India. The same happens after extensive clearing of forests when the land is not put under cultivation; it is said to be responsible for the increase of malaria in certain parts of Mauritius.

Arboriculture as an anti-mosquito measure.—With a view to drying the subsoil, trees have been planted on account of the great activity of the transpiratory function shown by growing vegetation and the consequent absorption of excessive moisture from the soil—the number of trees planted being in proportion to the needs and dimensions of the locality.

Special plants and belts of trees.—The most useful plants for anti-malarial arboriculture are those which grow most rapidly under the different climatic and geological conditions met with in a country. In the cultivation of such plants on a large scale, however, trees which will be remunerative should be chosen. Pines of various species have been used and recommended in India. Casuarina (*C. equisetifolia*) and Nim (*Azadirachta indica*) are the most useful and rapidly growing trees found in malarious districts. Chrysanthemum, sunflower (Helianthus), the beautiful plant Canna (N.O. Scitamineæ), castor oil tree (*Ricinus communis*), *kiri* tree, etc., also tend to dry the soil. It is possible that these particular plants may have some deleterious influence on the life of the mosquitoes, but most authorities consider this very doubtful.

Cutting down trees and cultivation of their site have rendered certain malarious places healthy. On the other hand, it is a well-known fact that the cutting down of copses and forests, without subsequent judicious cultivation of the denuded area, has transformed many large tracts of well-drained land into swamps and marshes. Trees should never be removed without thoughtful consideration as to the advantages and disadvantages of doing so. As belts or clumps, or even heavy shrubbery, placed between malarial localities and human habitations, trees have constantly been known to act as a protective agency against malaria. On the leeward side they help to filter mosquitoes from houses; open windows and doors on this side may be a danger. Mosquitoes enter houses in the evening and leave in the morning. Trees are natural interceptors of mosquitoes from their breeding-grounds. Large plantations of sunflowers have been reported to act in this way, but their efficacy is very questionable.

A belt of trees is some protection in screening mosquitoes from dwellings, but if too close to habitations it may be a danger by affording rest and shelter to these insects. On the other hand, it may be necessary to uproot trees when they are excessive in number, *e.g.* in areas where there are swamps and pools hidden from the sun by trees which prevent evaporation. In a few stations on the North-West Frontier, and in Assam and Burma, the writer was instrumental in having from 20 to 40 per cent. of the trees cut down; this was followed by improvement. But deforestation helps to reduce the rainfall; this may not always be an advantage.

The cultivation of blue gum trees (*Eucalyptus globulus* and *E. rostrata*) has not responded to expectations. They do not prevent mosquitoes living in their vicinity, but their rapid growth and the exceptional amount of evaporation from their leaves tend to lower the level of the subsoil water.

Trees with many rot holes should be felled or the rot holes filled up with cement.

Section 4—PREVENTION OF MALARIA IN HUMAN HABITATIONS IN INDIA

Under this heading it is proposed to deal with:

I. Prevention of Malaria in Towns in India; II. Prevention of Malaria in Villages in India; III. Prevention of Malaria in Schools in India; IV. Prevention of Malaria in Houses in India; V. Anti-Malarial Measures for Gangs of Labourers and Large Industrial Works in India; VI. Prevention of Malaria in Military Cantonments in India; VII. Prevention of Malaria in Jails, Asylums, etc., in India; VIII. Prevention of Malaria in the Individual in India

I. Prevention of Malaria in Towns in India

Radical changes in the health of a town are never the outcome of a single year's sanitary work, and the best results can only be achieved in towns where the work of sanitary regeneration is comprehensively, thoughtfully and scientifically carried out from year to year as the income of the municipality permits.

For various reasons referred to in Prevention of Malaria in Villages in India, malaria is less prevalent in towns than villages.

Anti-malarial committee in towns.—Every town should have its Anti-Malarial Committee, organised and worked in the way laid down under PREVENTION OF MALARIA IN VILLAGES IN INDIA (pp. 373–377). The scheme therein outlined, first inaugurated by Dr. G. C. CHATTERJEE, late Assistant Bacteriologist to the Government of Bengal, is one of the most laudable efforts ever made in India to attack and control malaria in that country in a comprehensive way. Initially the local municipality should appoint this committee from its commissioners, but gradually it should become an independent unofficial body selected by the people of the town.

Malaria can be reduced in most towns and cities in India in which it is endemic by sound sanitation, including well thought-out practical anti-malarial measures. It costs a town one way and another about four times as much to harbour malaria as to reduce it. In towns thoroughly and efficiently sanitated, and in which all breeding-places of Anopheles are properly dealt with, there should be little malaria; such sanitation almost automatically eliminates Anopheles. The only exceptions to this are towns surrounded and intersected by extensive swamps, and those within the zones swept by periodical outbursts of widespread *epidemic* malaria associated with flooding and other factors not well understood. On the other hand, there are whole towns in India which it would be a wanton waste of money and effort to attempt to render non-malarial. The following graphic description of the town of Thanesar (Punjab) represents what is meant:

> "Thanesar:—a dying ruined town, and spot of special Hindu sanctity and pilgrimage in the Punjab; raised on a hill produced by huge surrounding excavations kept full of water by annual inundation from mountain-fed rivers and swarming with larvæ of *Anopheles culicifacies*, *A. fuliginosus*, *A. sinensis* and *A. rossii*, the adults harbouring in ruins and jungle; peopled by Brahmins, living precariously on alms from pilgrims visiting the place in thousands at the time of a solar eclipse, and jealous of any suggestion of Western interference; cared for by a bankrupt municipal committee; possessing an average spleen rate of 61 and a malaria rate which has been as high as 50 per cent. Such is the problem facing the writers. The suggested solution is the abandonment as a town of this hyperendemic centre and its rebuilding on a site 3 or 4 miles distant, provided that annual inundation and intra-urban excavation can be eliminated." [1]

A properly sanitated town is a most inhospitable abode for Anopheles, just as the ordinary Indian village is one of its happy hunting-grounds. We have only to compare the health of the European parts of the presidency capitals with that of the villages in the environments of these cities to recognise this. The absence of *bustees* and *kinthals*, the presence of open streets and squares, good roads and drainage, dry and well-built houses that are properly ventilated, provided with electric fans or punkahs, in some cases screened with mosquito-proof wire gauze, in others fitted with mosquito nets, are conditions abhorred by Anopheles. We may be certain that in them the European is much less liable to the attacks of Anopheles than the inhabitant of an Indian village. "We must consider what is likely to happen to such insects as still might get into rooms so unsuitable to their taste. Are they as likely to bite human beings, or to light upon an infected human being, as they would be in a native village? Are they likely to remain in a situation so inhospitable long enough to develop an infection (ten to twenty days) if it were acquired? Such a favouring concurrence of events is likely to happen only where large numbers of Anopheles

[1] "Report on Malaria in Thanesar Town," by Lt.-Col. C. A. GILL and HARNAM SINGH, as abstracted in *Trop. Dis. Bull.*, Vol. 17, No. 2, February 14, 1921, p. 131.

and large numbers of infected human beings exist for a considerable time in constant association in an environment that suits the insect."[1]

Among the more important modern methods of town sanitation in the tropics are—complete drainage of the surface soil and subsoil, a good, constant public water supply that excludes storage of water in houses, screening of houses to prevent the attacks of adult mosquitoes, the prevention of breeding of mosquitoes in the town and for half a mile around it, and the bringing of all cases of malarial fever under effective quinine treatment as early as possible.

Drainage of a town.—In India the laying of a complete set of surface drains with house connexions forms the basis of all large sanitary measures. It is seldom possible to inaugurate such a system at once, but initially a definite, complete system should be planned in co-operation with an expert drainage engineer and an officer trained in tropical sanitary science, to be extended annually as funds permit. All drains should form part of the system, and must be sufficient to remove storm water and refuse water from houses, industrial works, etc. As a rule work should be commenced at the centre. Existing irrigation channels should be graded and extended where required to serve as outlets for storm water. If a *pukka* drainage system cannot be laid in old towns where *katcha* drains are already in existence, these must periodically be cleared, regraded, freed from vegetation and inspected.

Cesspools should be covered so as to render access of mosquitoes impossible, and they should be treated with kerosene oil once a week. Anophelines have been discovered near houses where no other breeding-places than cesspools could be found.

Public water supply.—The next most important factor is a modern, constant water supply conveyed in pipes, with hydrants and taps distributed along the streets, and, if possible, in the houses to avoid domestic storage. The closing of all private wells and the abolition of all house cisterns and tanks is an important part of this system, and caste prejudice should not be allowed to interfere with this being done when sufficient water is available for a constant supply. The drainage system *must* precede the water supply, for if the latter comes into the town and there is no definitely arranged outlet for waste, the result is the raising of the water table, which is exposed in every hollow as a pool, every pool forming a breeding-ground for anophelines. There are some large civil stations, towns and cantonments where neglect of the rule *drainage first, water supply next*, has led to severe endemic malaria, where malaria was previously of a mild type. It is imperative that the waste from the public water supply should be got rid of. Some sort of *pukka* platform or benching—glazed brick, concrete, etc.—should be laid in connexion with the tap or hydrant, the drain from which should communicate with the surface-water drainage system of the town.

It is also essential that the previous sources of water supply should be either abrogated or rendered harmless. All old and disused wells should be completely filled up, or effectually screened from mosquitoes. If a piped water supply cannot be provided and wells are the source of supply, they should be provided with pumps and covered.

A good piped water supply, the abolition of storage arrangements in private houses, and the closing of all private wells are among the most urgently necessary sanitary requirements in many towns in India.

No drains should be interfered with, or laid, or connexions made, without

[1] See an illuminating article by Lt.-Col. A. W. ALCOCK, C.I.E., F.R.S., I.M.S., "The Anopheles Mosquitoes in England," in *The Lancet*, July 4, 1925, p. 34.

the permission of the health officer or municipal authority, and none should be permitted that do not form part of the general accepted plan of the drainage of the town.

The difficulties in connexion with anti-malarial measures in a malarious town that is not provided with a public water supply and is undrained are very considerable. It has repeatedly been proved that malaria will undergo considerable reduction on the establishment of sound sanitation in a town—the introduction of a good water supply, a well thought-out drainage system, good arrangements for removal of excreta, good streets properly paved, proper rules for all new buildings, and a well-organised establishment for carrying out all sanitary measures required. Except within the zones of real epidemic malaria the persistence of intense malaria in large towns situated remote from marshes and river-banks is a positive indication of sanitary maladministration.

Cisterns, water-containers, etc.—Wherever reservoirs, cisterns, metal or other house tanks, barrels, etc., containing water are in use, even when these are underground, access of mosquitoes to the water should be prevented; the place of ingress of the water should be effectually screened with wire gauze. Roof cisterns are favourite places often overlooked. Periodical inspection is essential, at which time any defects in protection must be remedied. Mosquitoes do not like long, horizontally laid pipes, so that screening is unnecessary to pipes provided they are 12 to 15 feet long. Screening should also be carried out for all water butts, tubs, cans, buckets, kerosene-oil tins; otherwise they should be emptied at least once a week and exposed to the sun for a few hours. This holds good for all indoor and outdoor vessels containing water—native pots, water-coolers, *soorahies*. Water-containers are often hidden in out-of-the-way places; those not actually required should be removed.

Watering troughs.—Troughs built by municipal boards or charitable persons for watering cattle, horses and ponies at wells should be kept clean, and allowed to dry once a week for a few hours.

To sum up, the beneficial influences arising from a good public water supply as affecting malaria are now easily understood—it removes all the collections of water from miscellaneous sources, domestic cisterns, wells, etc., that had previously been in use. A good water supply, good drainage and proper conservancy of towns and villages are the sheet anchors for preventing malarial disease. Views as to their influence in reducing the incidence of malarial diseases have undergone no change in consequence of the established relationship between anophelines and malaria. Before the elucidation of the cause of malaria it was known that with these sanitary requirements places were either rendered free from malaria or this was greatly lessened. Present-day knowledge emphasises the necessity for these sanitary measures.

Paving and levelling of streets, roads and courts.—The surface of the streets, roads and courts should be hard, smooth and impervious. The material employed for the paving of streets for carriage and horse traffic is usually determined by that which is locally available, or what can be obtained at a reasonable cost. Macadamising and *kankar*[1] are mainly used. They crumble and leave holes in which water collects, but the latter of these collections are never used by Anopheles to breed in. Asphalt is inapplicable on account of the climate. The street should be highest in the centre and slope on both sides for drainage to the side surface drains or gutters. Uneven streets and roads should be levelled. The surface of all courts and open spaces not used

[1] Crude carbonate of lime, extensive beds of which exist beneath the surface crust of the soil over vast tracts of India. It is easy to quarry and is extensively used.

as gardens and recreation grounds should have a hard, impervious surface and be properly drained. Well-paved streets, roads, lanes, courts and squares prevent the formation of small puddles, runnels and pools during the rains.

Street gutters.—When these allow of collections of water, they must be properly graded and repaired.

Water-logging embankments.—When it is definitely known that an embankment seriously impedes the drainage of a thickly populated area, as shown by the much higher subsoil-water level, or a much larger number of breeding-places for mosquitoes, on one side than the other, then drainage is emphatically indicated. The openings through the road are either not large enough or not deep enough, both remediable causes (see Fig. 99, p. 350).

Excavating the soil and creation of borrow-pits.—Excavations have existed around Indian towns and villages from time immemorial and are to this day being created in all new towns and villages. Each house-builder finds the earth required for building, in the immediate neighbourhood of the house being raised. No excavation should be permitted within half a mile of the boundary of any town, or within a quarter of a mile of that of any village. Towns are liable to grow so rapidly that what is on the outskirts of the town to-day will, ten years hence, be well within its boundaries.

All existing borrow-pits should be dealt with as already indicated (pp. 360, 361) and the whole surface of the town should be levelled so that no water can collect.

Municipal by-laws should be in existence prohibiting the digging of tanks and pits below the natural drainage level; such excavations lead to stagnation of water within municipal limits and foster the breeding of mosquitoes. Low marshes and swamps in towns on and near the sea-coast may be filled up by pumping in silt or sand.

Removal and destruction of undergrowth.—All compounds should be kept free from undergrowth—rank jungle, weeds, brushwood and long grass—both on anti-malarial and on general hygienic grounds.

Trees near houses.—Trees should not be allowed in the immediate neighbourhood of houses in towns; they attract and shelter mosquitoes, give out moisture, exclude breeze, and reduce light. But trees along the boulevards of a modern town are healthy.

Sanitary inspectors.—Every place in which mosquito-breeding may by any possibility occur should be visited weekly by a sanitary inspector. Usually two sanitary inspectors can deal with a small town, whereas six or more each in charge of a definite section would be required for a large provincial capital. The sanitary inspectors should be provided with the equipment laid down for searching for larvæ on p. 90.

The first investigation of any premises by the sanitary inspector should be deliberate, and detailed notes made of defects discovered. The inspector tells the inhabitants why he has come and points out any actual or potential breeding-places for mosquitoes; with tact and civility he insists on these being done away with. He tries in every reasonable way to persuade them to take in hand the measures at their disposal that will reduce their malaria. He may catch some larvæ; show them to the tenant, and explain the danger of allowing them to breed in and near the house; ask people to empty all barrels, chatties, etc., twice a week, and to screen them when they contain water. Explain the part played by broken bottles, crockery and earthenware utensils, empty tins, old buckets, flower pots, etc., in the breeding of mosquitoes. These should be removed from houses to dustbins, and then to incinerators or buried, tins being first perforated. He leaves an anti-malarial

leaflet,[1] explaining, where necessary, its contents. If he observes any condition that he considers should be handled by the mosquito brigade, such as a pool in a street ditch that calls for draining, emergency oiling to prevent early hatching of many pupæ, etc., he makes a note of it, and on return to the office he prepares on suitable slips of paper a work order form, such as is used in all large municipalities. At the end of three days the inspector should return to the houses inspected, and if the work ordered has not been done, he consults the M.O.H. as to whether complaints be laid. If a charge is laid, the inspector must appear as a witness at the time the court directs. Until the M.O.H. knows the sanitary inspector, and can rely on him, he should see the premises himself, to be certain that the situation falls within the scope of the by-laws, and that the work prescribed by the sanitary inspector is reasonable.

It is, however, a sound rule not to have recourse to the law until all other means have been exhausted; co-operation of the people, not coercion, is required. Never prosecute unless the case is strong, and then press for exemplary punishment. It is a warning and a lesson. Too many prosecutions will arouse antagonism to anti-malarial campaigns. In the writer's experience as health officer of a very large municipality for ten years it usually seemed wiser to enter into some sort of a compromise with the tenant that would ensure the work required being carried out. Many a time he has spent a whole hour in the law court, at the end of it the delinquent being let off with a caution or a fine of 1 anna!

Other intra-urban water.—A special branch of the sanitary staff should be daily and continuously employed in systematically treating every pool, pond, tank or drain breeding Anopheles with petroleum, and in such a manner as to cover the whole surface of the infected water lying in it once a week during the breeding season of anophelines. The adoption of this measure should be supported by power to prosecute the occupier of any premises on which mosquito larvæ are found. Such legislation now exists in various malarious countries. The sanitary establishment of towns should see that owners and occupiers of houses and land keep their premises free from mosquito breeding-places; keep water-courses and flood-water drains and culverts clear, properly graded, in good condition, and free from vegetation, and if pools are found in them apply petroleum; clear away undergrowth, long grass and jungle within the boundaries of the town, and make arrangements for clearing the land outside the municipal boundaries for 500 yards; fill up or drain excavations, pools and low-lying lands, where water is likely to lodge. When marshes at the foot of small hills are not due to seepage, and material from the hill can easily be obtained, it should be used to fill up the marshes, borrow-pits, etc. When this is done, care should be taken in regard to levelling the area from which the earth is removed. The municipality should limit the number of open drinking-water tanks compatible with a sufficiency of supply, and provide special tanks well removed from huts and houses for washing and bathing purposes.

Constant supervision and education are necessary to protect the inhabitants against their own negligence, indifference and ignorance, and to inculcate the habit of self-care.

Plans and site plans of all buildings to be erected should meet with the approval of the health officer or municipal authority.

Swamps, etc.—When *marshes in the immediate vicinity of towns* cannot be permanently dealt with by drainage or filling they should be oiled regularly, or converted into ornamental water tanks with *pukka* sides.

"Wet" cultivation.—No kind of "wet" cultivation should be allowed

[1] A suggested leaflet is contained in App. I.

in towns, and rice should not be grown within half a mile of the outer boundary, and then only if adequate arrangements are made for the effluent from the fields.

Education in anti-malarial measures.—The inhabitants should be simply educated in the relation between mosquitoes and malaria, the value of quinine in malaria, the construction of their huts, general and anti-mosquito sanitation, and hospital or dispensary figures should be regularly published. It would be useful to post in a public place a monthly graph of the health of the town.

Periodical malaria survey.—The amount of malaria in the town should be estimated periodically by ascertaining the parasite rate, spleen rate and sporozoite rate to gauge the results of anti-malarial measures; a regular and progressive increase will call for some change of the measures being adopted.

Regulations.—Certain by-laws connected with anti-mosquito work should be published and enforced by the town or city council, such as those detailed on pp. 249–251 and in Appendix III.

Table of minor anti-mosquito sanitary works in towns.—The sanitary inspector or other responsible person should report daily to the municipality or health officer the following points on a printed form:—[1]

	Sanitary Divisions.					
	1	2	3	4	5	6
1. Number of inspectors employed						
2. Do. houses inspected						
3. Addresses of houses where larvæ were found						
4. Number of notices served to remove conditions causing the breeding of larvæ						
5. Number of prosecutions attended						
6. Number of work orders issued						
7. Number of persons fined for having mosquito larvæ on premises						
8. Number of linear feet of ditches cleared						
9. Do. do. dug and graded						
10. Do. square yards of weeds, grass and vegetation cut and removed						
11. Do. excavations filled up						
12. Amount of low-lying land raised						
13. Number of cubic yards of material used for filling up excavations						
14. Number of men employed for 8, 9, 10, 11, 12 and 13						
15. Number of persons fined for making new excavations without permission						
16. Number of drains oiled						
17. Do. pools ,,						
18. Do. tanks and barrels oiled						
19. Do. men employed for oiling water tanks, barrels, drains and pools						
20. Other places inspected						

The reports should be verified and some responsible officer should see that the work is done regularly, systematically, fairly, and with judgment. If there is a malarial medical officer, he should, of course, keep up this record,

[1] Adapted from Sir W. J. SIMPSON's *Principles of Hygiene as Applied to Tropical and Sub-Tropical Climates*, p. 375. In preparing the section on PREVENTION OF MALARIA IN TOWNS IN INDIA the writer has been much indebted to Sir J. W. SIMPSON's valuable manual.

otherwise the health officer should do so. This daily record indicates, *inter alia*, how far the community is co-operating.

A complete record of everything done by the anti-malarial staff should be kept. Each overseer and sanitary inspector should maintain a table giving a daily *time summary* of those working under him, and also a *working summary*, showing the kind of work done and the details regarding it—where carried out, amount of petroleum used, places stocked with fish, etc.

Maps of the town divisions should be in possession of all the staff concerned. A scale of 1 inch to 200 or 400 feet is best. Several copies are required. One should show all the topographical features bearing on mosquito-breeding as found during a previous complete malaria survey. As all old ditches and channels are cleared, regraded and trained, as new ditches are completed, as marshes are drained, as hollows, borrow-pits and holes are filled up, as ponds, streams, etc., are stocked with fish, as oil stations (p. 316) are formed, they should be suitably shown on the map by symbols or otherwise, the meaning of the symbols being entered in the margin or at the foot of the map.

A map on which places that require oiling and position of the oil stations are shown should be in charge of the oiling overseer. Another showing places—pools, streams, swamps, etc.—that are suitable for larva-eating fish should be given to the overseer in charge of fish control. A map is also required by the overseer in charge of ditch maintenance to indicate position of ditches. Each overseer will, of course, have a map or plan defining his section. Lastly, the malaria officer or health officer will have for reference in his office a map of the town giving all the details mentioned in the overseers' maps, and including the statistical data required to use it as a "spot map" as regards local malaria (see p. 408).

For details regarding town *petrolege* see pp. 313–318. For details regarding fish control of mosquitoes see pp. 322–327. For measures of defence against adult mosquitoes, see pp. 299–312. It should be remarked, however, that the screening with wire gauze in towns and villages is inapplicable to quarters occupied by the uneducated and lower classes. Screens are delicate structures, require care, and must be kept in a good state of repair. A defectively screened house or hut is a mosquito trap which allows mosquitoes to enter and keeps them in. The sanitary education of the masses must be much higher than it is before screening can be recommended for them.

Treatment of malarial fevers.—Means of attack upon the parasites themselves may be made a most important feature in a campaign against local malaria. Discovery and treatment of all malarial infection, active or latent, should be aimed at.

In cities and larger towns it is desirable to establish one or more malaria clinics, at which medical men and women working in the area should receive tuition from an expert on malaria, qualified to give special instruction and demonstrations. These clinics should be organised as malaria diagnosis centres with the intention of bringing under quinine treatment all cases of malarial infection discovered.

The people themselves should be instructed by popular lectures, cinema films, placards, health visitors, and in other ways.

Every possible facility for the proper treatment of malaria cases, who desire to avail themselves of it, should be provided, by means of hospitals, out-patient dispensaries, and adequate arrangements for the distribution and use of quinine or cinchona febrifuge. Specially low prices for State-manufactured quinine and cinchona febrifuge might well be offered to charitable medical institutions.

Further anti-malarial measures are referred to under PREVENTION OF

Malaria in Villages in India and Prevention of Malaria in Houses in India, pp. 373–377 and 378–382 respectively.

Town mosquito brigades and gangs.—A mosquito brigade is one of the best methods of dealing economically with limited areas of endemic malaria, and should be arranged in every municipality so situated. The brigade should work on the general lines already indicated. The personnel should be sufficiently numerous to cover the allotted ground weekly. In an ordinary Indian town it may be said that a brigade of fifteen men and one headman should be able to work over an area of one and a half square miles.

The duties of the mosquito brigade men are :—to visit regularly, once a week, the compound of every house in the town, and do away with every pool and other collection of unnecessary water which can harbour mosquito larvæ; to oil every collection of water which is too large to be destroyed; to remove all broken tins, pots, bottles, etc., which can contain water and harbour larvæ; to keep roadside ditch drains, *nullahs* and water channels, margins of ponds and streams clear of weeds and obstructions; to fill up small holes and pits with earth, etc.; to instruct the inhabitants in the recognition of mosquito larvæ and the methods of destroying them; to see that the by-laws requiring that all fixed receptacles of water, cesspools, etc., should be made mosquito-proof are carried out and to bring to the notice of their superiors every householder on whose premises mosquito larvæ are frequently found; during the rains to drain off quickly all superficial collections of water which can last sufficiently long to become breeding-grounds of mosquitoes; to endeavour to kill adult mosquitoes in houses, outhouses and stables by fumigation with sulphur dioxide or by other means; to make observations on the seasonal prevalence of mosquitoes and their habits, and on every matter regarding which increased knowledge might aid in the extermination of these insects.[1]

The anti-malarial duties of the sanitary inspector should consist of organisation of the mosquito gangs and allotment of their tasks, supervision of work of assistant sanitary inspectors, overseers and other subordinate staff, checking of reports, issuing notices to abate mosquito-breeding places, identification of mosquitoes and mosquito larvæ, attendance at court, etc. The routine inspections of the assistant sanitary inspectors for detection of larvæ, oiling, etc., should be so arranged that the town is covered in a week, and all houses and yards visited. When larvæ are found they should be collected; the labels should show the name and address of the occupier of the premises; orders to get rid of larvæ should be signed by the M.O.H. or sanitary inspector.

In an endemic locality anti-malarial work should never cease; even in the Panama Canal Zone, with its perfected system of anti-malarial sanitation, it is still found that any relaxation of vigilance is followed by increased incidence of malaria. The necessity for perpetual anti-malarial propaganda throughout the town should never be lost sight of.

The expense of anopheline reduction in towns is relatively small per head of population, seeing that the expenses of case reduction are proportionate to the density of population and not to area.

II.—Prevention of Malaria in Villages in India

The reduction of malarial diseases of villages is one of the most important economic questions of India. It is likewise one of the most difficult matters to accomplish, chiefly on account of its vastness, and because of the ignorance and poor circumstances of the rural population in general, and the absence of

[1] Lt.-Col. S. P. James, I.M.S., *Malarial Fevers*, 3rd Ed., p. 93.

doctors and educated people to advise the rural population as to how to prevent malaria. There are about half a million villages in India.

Four-fifths of Indian malaria occurs in villages.—Probably about four-fifths of the malaria of India occurs in villages and rural districts. The proportion of persons attacked in the Army in India is, we know, about 20 per cent. A similar proportion in the civil population would mean that in the latter there are 65 millions of cases of malarial fever annually. Allowing that there are 15 millions placed under treatment in one form or another, there are left 50 millions who never get any treatment on Western lines; 75 millions, and not 50 millions, would roughly represent the untreated cases (see pp. 12, 290, 291 and App. I.). We might argue that these victims are working out an immunity for themselves, but such a doctrine does not aid us in solving the problem of prevention of rural malaria, and it leaves unconsidered the question of the millions of infants and children who die from malaria while on the way to develop immunity.

In the Indian village of some Provinces (parts of Bengal, for instance) located on land with a very high subsoil-water level, leading to water-logging, and without drainage, the irregular surface gives rise to ponds or temporary pools in which Anopheles breed, supplementing the permanent collections formed by old excavations. Villages are in most places surrounded by jungle and scrub. *Bustees* and *kinthals* built of sun-dried brick, and covered with thatch, damp, dark, and ill-ventilated, with domestic water-containers, form a paradise for the winged anopheline. "In such conditions the villagers and the Anopheles live together in close intimacy, and the swiftly succeeding swarms of Anopheles must always be sucking the blood of infected human beings and returning the infection indiscriminately to the village population." [1]

Special measures recommended for villages.—There are several special measures which are recommended for all villages in the more severely endemic malarious districts: (1) Discovery and treatment, with quinine or cinchona febrifuge issued gratis or at a low price, of all cases of malarial fever and malarial enlargement of the spleen; the house-to-house visitation to find the cases should be arranged by the village headman. (2) The making of surface drains, properly graded (even *katcha* drains), for removing storm water, rain-water and refuse water generally to the nearest natural outfall, the work being done by the villagers under an overseer. (3) Covering of all sources of water supply with some mosquito-proof material—this material can often be manufactured by the villagers from local sources. (4) All useless rubbish-tins, chatties, broken bottles, etc., which will hold water, should be destroyed or buried; the filling up (or preferably draining, where this is practicable) of all borrow-pits and excavations in the village, and outside it for a radius of at least 100 yards. Pools not absolutely necessary for watering animals or for domestic purposes should be drained or filled up; when this is impossible, they should be oiled once a week. (5) The prevention of cultivation of all dry crops within 100 yards of the village, and of wet cultivation within 200 yards. (6) The keeping of the 100-yard area and the interior of the village free from mosquito larvæ; this should be carried out by the villagers, a group of three of whom should take it in turn weekly. (7) Education of school children as to the nature of malaria, its relation to mosquitoes, how to reduce these insects, and the use of cinchona febrifuge and quinine in malaria. The school teacher should issue quinine or cinchona febrifuge tablets to children suffering from malarial fever. Village schools should be visited periodically by some medical authority, and cases of malaria discovered brought under cinchona febrifuge or quinine treatment. (8) For a distance of 100 yards around the village jungle and scrub should be cut down

[1] Lt.-Col. A. W. Alcock, C.I.E., F.R.S., I.M.S., in *The Lancet*, July, 1925, p. 34.

and burnt *in situ* at the commencement of the summer or end of the rains (p. 311). (9) When the subsoil water is high adequate arrangements should be made for draining the soil, so that it may remain dry in the village and its immediate neighbourhood (pp. 333-330). The villagers should do whatever ditching or laying of subsoil tile drains may be necessary. (10) The village agriculturists, especially in rice-growing districts, should leave the fields before sunset to avoid the attacks of anophelines. (11) The path to the watering place at the village pond for cattle and other animals should be paved. Where there is no pond, and the water supply for animals is from wells, the wells should be connected with watering troughs, which should be allowed to dry completely for some hours once a week. (12) Distribution of illustrated leaflets written in the simplest local vernacular, to be explained by the headman of the village, and maintenance of anti-malarial propaganda as continuously as possible are helpful. What is of the greatest value is to get at the people directly, and show them that we are profoundly interested in reducing their malaria and other diseases. The issue of malaria pamphlets and of circulars couched in technical terms is of no use whatever to the uneducated masses; besides, these dissertations, on reaching the village, find their way to the *thana* or headman, and are filed with other documents. (13) The villagers should be told repeatedly of the great use of hand destruction of adult mosquitoes and how to use butterfly nets for the purpose; these nets they can make for themselves.

The incidence of malaria in rural areas can be lowered by reduction of the number of Anopheles; it is only in very exceptional places that such reduction cannot be effected, especially if the individual and the local community in each place co-operate in carrying out the required anti-mosquito operations.

There are thousands of villages where malaria is kept up by a few breeding-places of Anopheles, either in the villages or on the immediate outskirts. In a large percentage of these, simple anti-mosquito operations, carried out by the villagers, are sufficient to rid the inhabitants of their malaria. It is not often that large drainage or filling-in schemes are required in villages.

What is being done by Provincial Governments to control malaria in rural districts?—Apart from the field work carried out by the civil surgeon and his subordinates in rural districts, Provincial Governments have of late years maintained *travelling dispensaries*, and used *demonstration camps* to educate the villagers in anti-malarial work and teach them the value of cinchona febrifuge and quinine in malaria. Working in association with these two, in some Provinces, is a *field laboratory*.

The purpose of these *demonstration camps* is to educate the people regarding malaria, the methods of its prevention, and the use of quinine. The work is generally in the hands of assistant surgeons and sub-assistant surgeons, who are engaged mainly in treating the sick. The circle unit contains about 2,000 people. The sub-assistant surgeon visits each village twice a week, searches for the sick, and treats them; those suffering from fever are treated by quinine or cinchona febrifuge. At the end of two months the camp moves on to another area of the same size in the neighbourhood, until the whole district has been covered. The sub-assistant surgeon in charge of the circle keeps a register on the fly-leaf of which is printed a set of rules for his guidance.

The assistant surgeon supervises and inspects the work of the sub-assistant surgeons and their compounders by frequent visits, and endeavours to interest the people in the scheme by his personal influence. He keeps a diary and a register in which he enters a summary of the sub-assistant surgeons' registers, and the stock of medicines for distribution. Each sub-assistant surgeon is provided with two tents and with a compounder to assist in the preparation of the medicines.

The *field laboratory* is brought into operation when the demonstration and test camps are organised and working. Antecedently men are trained in collecting

mosquitoes, and in examining areas in which Anopheles breed, in taking spleen rates of children, examining blood films for parasites and other work.

The foregoing is a brief account of an anti-malarial campaign in the villages of selected districts in Eastern Bengal and Assam organised by the Director of Public Health, Lt.-Col. E. C. HARE, I.M.S. Something similar is carried out in other Provinces with much benefit to the village population. The areas visited must necessarily form but a very small part of the endemic malarial foci of rural India. Until some such organisation as that referred to in the following paragraphs comes into existence, *travelling dispensaries* should be working all over India.

Until recently little has been done to control the malaria in villages; that is to say, only very limited rural areas could be attended to. It is too prodigious a task to be dealt with effectually by Provincial Governments. It should be undertaken by the indigenous community. A praiseworthy and comprehensive scheme for combating malaria in the Province of Bengal, a highly endemic region, was inaugurated by Dr. G. C. CHATTERJEE, late Assistant Bacteriologist to the Bengal Government. In 1918 he started his scheme in three villages which had been decimated by an epidemic of malignant malaria. He organised three Co-operative Anti-Malaria Societies, and got them registered under the Co-operative Societies Act. Later he founded a Central Co-operative Anti-Malaria Society to " devise and carry out measures based on co-operative principles for the eradication of malaria from Bengal, which was registered and brought into being on June 5, 1919." Sketched briefly the scheme is as follows:

" The Central Society exists to organise and create a network of Anti-Malaria and Public Health Societies on a co-operative basis throughout the villages of Bengal. Each of these societies is an autonomous body which raises funds by subscription from amongst its members. The Central Society acts as an advisory body to these rural societies, and may assist them financially. It places at their disposal the result of recent researches on malaria, kala-azar, cholera and other preventable diseases. By February, 1924, as many as 129 societies had been organised. The anti-malaria measures which a society is required to carry out are: (1) filling up ditches; (2) improving drainage; (3) preparing a map of stagnant pools and regularly kerosinating them by volunteer help; (4) clearing undergrowth in the village; (5) administering quinine to all malaria cases in the village; and (6) keeping the fever index of the village systematically. Each society provides a duly qualified medical practitioner on a subsidy basis, whose duty it is not only to treat cases of illness, but also to instruct the people in preventive methods, and to establish a co-operative dispensary in the village itself or within easy reach of it. For organising public health societies and for educating their members, the Central Society carries out propaganda by means of magic-lantern lectures, leaflets and a monthly journal, while the cinema and the stage are also pressed into service. The society is very strongly supported by the medical profession. Not only do the majority of its members belong to the profession, but it has also enrolled about 180 medical volunteers, at least half of whom are fully qualified practitioners, the rest being senior medical students. It enjoys good financial support, including a grant from Government, which in 1921 and 1922 was Rs. 5,000 and in 1923 Rs. 10,000. The organisers of this system are to be heartily congratulated on their efforts to awaken the sanitary conscience of the village population of Bengal, and to promote the idea of self-help in local sanitation. It is to be hoped that such methods will in the near future be more widely extended throughout India." [1]

Nothing with such potentialities for good in the control of malaria has hitherto been attempted in India. Carried out in its integrity it must effect a considerable reduction of malaria in the Province of Bengal, and if universally introduced in India would materially affect the malaria problem. It is earnestly hoped that the ideas incorporated in the scheme will be put into practice in all

[1] *The Lancet*, April 25, 1925, p. 891.

parts of India. The writer would make one comment; it is connected with the economic aspect of quinine in the scheme. The scheme, if it extends, must greatly increase the demand for quinine and cinchona febrifuge, and with that increase the price will rise considerably. It is necessary to be prepared for this by the manufacture of larger quantities of these drugs in the Government factories. Unless the manufacture, administration and sale are under Government it will not be possible to keep the price down.

Notwithstanding all the difficulties to be contended with, the writer has long been confident that a great deal may be done to lessen the incidence of malaria and reduce anophelines in villages by the villagers themselves, and by pointing out to them the way in which they can reduce village malaria. If we wish to make a radical impression on the malaria of India we must attempt the enormous task of attacking this local infection in its rural home.

III.—Prevention of Malaria in Schools in India

Site of school.—Schools, where practicable, should be on an elevated site to provide for good drainage. They should be well lighted and ventilated. The school premises, including the playground, should cover half an acre for every two hundred pupils, be located remote from swamps, water-courses, open drains, ponds, pools, tanks and other collections of water. The compound should be free from borrow-pits and excavations. Schools should be centrally placed, off the main streets, and away from heavy traffic.

The teaching in schools of the nature, causes and methods of prevention of malaria.—The acquisition of a knowledge of the nature of malaria, its effects on the human body, and the rôle played by mosquitoes in its dissemination should be an essential part of the education of all school teachers, including those of the elementary schools. These teachers should also, as part of their routine duties, endeavour to impart their acquired knowledge to the uneducated adult population of the villages and towns in which they work. The main facts connected with the causation and prevention of malarial fevers should be taught in all elementary and secondary schools. These might be posted up on placards printed in the local vernacular, with illustrations of malaria parasites, and of adult anophelines and their larvæ (App. IV).

Free issue of cinchona febrifuge or quinine in schools.—One of the most comprehensive methods of dealing with the endemic malaria of India is that of endeavouring to eradicate malaria parasites from the blood of all school-going children by the curative use of quinine. We have already seen that children are the main source of all malaria in India, and that in endemic malarial districts a very large percentage of children from early infancy to ten years of age harbour malaria parasites in their blood. The school-going age may be said to be between five and fourteen years, and the writer would apply the system of free quinine distribution to all infected children up to the age of ten years. By the systematic use of quinine in schools, all infections and re-infections in these children would be cured and the amount of residual malaria in the country considerably lessened.

Method of distribution of quinine to school children.—The method by which this may be carried out is part of the general system of quinine distribution which the writer has advocated for malarial districts. The quinine should be issued in tablets to the schoolmaster for administration to all children. He should keep a register with a nominal roll of all children having enlargement of the spleen and all who are taking quinine. Throughout the malarial season

all school children suffering from malarial fever and those with enlarged spleen should get a dose of quinine according to age every morning for three months. At the end of the malaria season the schoolmaster should send a summary of the facts of malaria cases recorded in the school register to the malarial authority of the Province or District or other official appointed to receive these reports.

Lt.-Col. J. D. Graham, C.I.E., I.M.S.,[1] Public Health Commissioner with the Government of India, has shown that in endemic areas, when the spleen rate is higher than 50 per cent., the regular administration of quinine in schools has no material effect on that rate, but when the malaria is less severe, or where the malarious season lasts only a few months, quinine regularly given does reduce the spleen rate.

All schools should be subjected to periodical medical inspection. A Government Act is called for to form an educational medical service on the lines of that established in England, to inspect and periodically report on the sanitary state of schools and on the health of the school children.

IV.—Prevention of Malaria in Houses[2] in India

Site and construction of houses.—The Malaria Commission of the League of Nations, and in particular Lt.-Col. S. P. James, I.M.S., have pointed out that, at least as regards *A. maculipennis* in Europe, infection is, with the rarest exceptions, acquired in a house; so that in the prevention of malaria the house is of prime importance. This applies equally to India, except that other species of Anopheles are concerned, and that they may fly to houses from bazaars and other places where live those who are hygienically backward and careless.

As regards the site of the house, the neighbourhood of marshes and other breeding-places of mosquitoes that cannot readily be abolished should be avoided. Houses should be orientated to get the best effect of the wind. High winds, however, predispose to chills. Elevated situations should be sheltered by trees at a distance and not in the immediate neighbourhood, or by higher ground. Dryness of the site is essential; rising ground facilitates drainage. A porous soil is very desirable; "made" soil is condemned. The water table should, if possible, be 8 feet below the surface. Where the subsoil water is high and cannot be drained on account of the expense, cultivation of rapidly growing trees is advised; local experience as to the best for this purpose should be sought.

Houses in malarious localities should be constructed with special precautions. During the last hundred years in India in malarious districts there has been little change in the building of new houses, or in the restoration or rebuilding of old ones. The great importance of dry, well lighted and ventilated houses in India is not even yet fully recognised, although it has been brought prominently to public notice by many expert sanitarians. In such houses anophelines will not flourish. Until the last few decades every large cantonment on the plains and every civil station had one or more specially malarious houses with bad reputations, and there are still many houses of this kind in existence. The dwelling-room should be raised several feet above the ground level by a plinth or on arches. The servants' quarters should be in separate buildings, away from the house, and European quarters generally should not be in the vicinity of native habitations.

[1] *Progress Report on School Quinisation*, 1914.

[2] The houses referred to are those that would be occupied by intelligent people in moderate or well-to-do circumstances.

Whenever possible the house should consist of two stories, in which case the ground floor should not be used as the sleeping-room. The bedroom doors and windows should be away from flower-beds and vegetable gardens. The walls should be covered with some light-coloured wash or light-coloured paper—light colours are not favoured by mosquitoes. Avoid unnecessary furniture and curtains, open clothes cupboards; have as few hanging clothes as possible; keep boots in a closed boot cupboard.

The cost of drainage and other extensive anti-mosquito work about isolated houses in malarious districts is seldom repaid; moreover, such work may be of doubtful efficacy, especially on or near swamp land. A much more suitable measure would be making the house mosquito-proof by screening. A house surrounded by marshes is at best a dangerous abode. Unless compelled by imperative reasons to occupy it, such a house had better be vacated or abandoned or only used as a day residence. If a house must be built on swampy land, the soil of the area should first be satisfactorily drained, if this is at all practicable.

Mosquito-proofing of houses.—In the planning of houses the part played by anophelines in disseminating malaria should be borne in mind. Houses provided with wire gauze to doors, windows and other openings through which mosquitoes can gain entrance and exit are protective against the attacks of these insects (see pp. 299–302 and Fig. 72).

Watering arrangements for gardens.—In most inland small stations in India the house garden is watered by means of water drawn from a well, usually by bullocks, the water being raised in a leather bag or bullock's skin, or by hand. It then flows into a channel to one or more cisterns from which either minor channels run to the different beds, or the water is carried from them in buckets, pails or garden cans. The bullocks, as a rule, work only for a few hours in the day, so that the cisterns have to be filled for the daily storage of the water. This distribution of cisterns is to economise the labour of the gardener in carrying the water. These small cisterns form some of the commonest breeding-places for mosquitoes in all stations, and especially in private houses.[1] *A. subpictus* larvæ are frequently found in them, and occasionally those of *A. stephensi* also. When used they should be provided with a well-fitting cover, permitting of access to the water, or they should be emptied once a week and kept empty for several consecutive hours during the daytime, or kerosened weekly.

Irrigation channels, large and small, especially when *katcha*, with banks irregular and not kept clear of grass and weeds, are popular breeding-grounds for anophelines, and, if possible, should not be allowed near private dwelling-houses. They, moreover, lead to heightening of the subsoil-water level with all its risks. Irrigation channels in gardens and compounds will breed Anopheles if kept full. They should run only for a few hours daily, and be allowed to dry completely between. No seepage should be permitted, and if irrigation is from a well, and there are collections of water in intermediate cisterns, these must be completely emptied or oiled weekly. Within his compound the owner or tenant is responsible for these. They cannot be considered nuisances, and compulsory drainage cannot be insisted on. In the case of swampy areas within compounds the owner or tenant is directly responsible that they are not breeding-places for anophelines.

Pools, tubs, etc.—All pools and ponds harbouring anopheline larvæ should be oiled weekly. Many pools can be easily filled up and the surface turfed or cultivated. If the irrigation supply is the only available

[1] Lt.-Col. G. GILES, I.M.S., *Health and Climate in Hot Countries*, p. 100.

source of water for the garden, all the channels distributing it should be *pukka*.

If tubs or other water-containers are necessary they should be covered with wire gauze and emptied once a week or regularly kerosened. They should on no account be kept in the house. They are one of the most frequent abodes of mosquito larvæ.

In the hot, dry season of the year there should be no breeding-places in or around houses. At this time all breeding-places are artificial, and with a little attention breeding can readily be prevented. Nevertheless, the writer has seen culicines in such vast numbers at this time as to be a pest.

Covering of wells.—All wells should be covered or made mosquito-proof. It would be a decided advance were all wells of Indian houses covered and provided with pumps. Disused wells should be filled up or properly screened.

Roof drainage.—Depressions in the roof of the house should be levelled. The drainage from the eaves should be into shallow drains around the bungalow, or brought into communication with the general drainage system (where such exists) and properly trapped. All gutters on roofs should be properly graded and kept in a state of repair.

Refuse water.—Water from bath-rooms and cook-houses should be conveyed away from the house by means of proper drains; it should not be allowed to flow over the ground in the neighbourhood of the house. All houses should be provided with a well-laid surface drain running around them, to carry away all water to the main or sub-main, and so prevent pools forming. All cisterns and tanks in connexion with houses should also have a drain round them. Such drains should be brought into connexion with the surface drains beyond the compound. All outhouses (servants' quarters, kitchens, etc.) should also be provided with proper drains.

Filling up of hollows and borrow-pits.—All hollows should be filled up or drained. It is often a question as to where to get earth to fill in hollows. As a rule there are some slightly elevated plots in a compound that may be levelled and the earth used for filling; or the earth bank of a compound wall may be used. Earth walls of this kind only serve to obstruct drainage without serving any practical purpose. Where no available earth is at hand, it is possible to lower the general surface level a few inches without harm and use the material for filling up depressions and holes. No excavations of the soil should be allowed.

One of the most useful ways of emptying water from large hollows or borrow-pits is to cut a narrow channel leading from the hollow to the nearest surface drain. Where a number of such small depressions lie close together they may be drained into the largest and this kerosened if it cannot be emptied or filled up.

The entire area around the house should be carefully inspected after a brisk shower of rain. It will then be noticed where water collects. These spots should be marked, filled up and properly levelled.

A good way to protect a house from the dust and glare of the hot weather is the maintenance of a well-kept grass lawn with a few trees around the compound, the latter, however, at a distance. The fewer the flower-beds the better. Flowers in verandahs give shelter to mosquitoes. The lawn should not be flooded with water, but sprinkled with it once a day; vegetation near houses gives out moisture and increases humidity, which is favourable to mosquitoes. Where a grass lawn cannot be kept up, a good hard, paved or gravel surface is the best substitute. In malarious places it is not wise to

have trees immediately around houses, for during the day they harbour mosquitoes, which in the evening get into the house through the doors and windows, especially when the rooms are lighted.

Cutting and burning of jungle and scrub.—See p. 311.

Screen of trees between house and swamp.—See p. 365.

Supervision of anti-mosquito measures.—The anti-mosquito measures around a house are easily supervised. All that is necessary is a walk round the house, compound, servants' quarters, out-offices, etc., once a week to see that the permanent orders regarding the prevention of breeding of mosquitoes are carried out—that all the garden cisterns, tubs, barrels, and all collections of water are emptied and cleaned out once a week. Any fresh breeding-places discovered should be abolished. Mosquito larvæ will not thrive in comparatively sterile water, and they cannot withstand the action of the direct rays of the sun for a few hours. This small amount of trouble will go a long way towards preventing malaria, to say nothing of adding considerably to the comfort of being free from the attacks of mosquitoes. Where people in a town or a group of adjacent houses work together, it is possible to lessen considerably the number of mosquitoes in the houses.

Legal responsibilities of tenants.—In private houses that are rented, the expenses which occupants are prepared to undertake will naturally depend on the length of time for which the house is to be occupied. Most officials in Indian stations are only temporary residents and will, as a rule, find it cheaper to adopt temporary measures, such as oiling all small collections of water. Where, however, people are more or less permanent residents, such as business men in large presidency and provincial towns, it will be found that a moderate outlay on permanent anti-mosquito measures is preferable to temporary expedients.

It is necessary to impose penalties on those on whose premises mosquito larvæ are found. "The prevention of mosquito-breeding should, however, be expected, not from infliction of penalties, but from organised work undertaken by the sanitary department. The penalties should only be inflicted on those who are obstructive, and even then only after the work has been so long in progress as to give the population an opportunity of being educated to its work."

Isolated farm-house or group of farm huts near a marsh or swamp.—The best measure is to drain the swamp (see pp. 345–349). If this is not practicable, then there are several things that can be done in addition to screening (p. 299 *et seq.*) and elimination of breeding-places about the house; the more important of these are:

1. Cut down all jungle scrub, tall weeds and grass harbouring mosquitoes. The surroundings of the house should be free from jungle and brushwood of any kind, and open to the sun and wind.

2. A screen of trees should be planted at a distance from the house between the swamp and the house. This hides the lights of the house from the swamp, and stops mosquitoes brought by breezes from their breeding-places.

3. Stock the parts of the swamp adjacent to the house with larva-eating fish.

4. Oil the parts of the swamp unsuitable for fish control once a week or use a few submerged oiled gunny bags, etc. (pp. 317, 318).

5. Build the bullock byre or stable between the house and the swamp, as far from the former as practicable. If the bullock byre or stable is already built in the wrong direction in relation to the swamp, or there is none and such cannot be erected, then pasture the cattle or other animals between the house and the swamp. This, however, is of doubtful value.

6. Make use of some mosquito repellant substance in the house, preferably kerosene on the floor and walls.

7. Kill all adult mosquitoes that are found in the house or that evade the screens (pp. 306–309).

8. Periodically smoke out all mosquitoes, or having by smoking concentrated them at one outlet, destroy them (pp. 308, 309).[1]

V.—Anti-Malarial Measures for Gangs of Labourers and Large Industrial Works in India

Special measures advocated.—The anti-malarial measures to be adopted for all gangs of labourers or for a labour force, and on all large famine relief works, require in each instance to be thought out after thorough local inspection and consideration of the numbers and classes of labourers concerned. The site of the encampment should be selected with care. Such preliminary malarial survey will soon compensate for all extra outlay on initial anti-malarial measures.

The area to be occupied by the work-people should be parked out, and cleared and levelled for 200 yards beyond building sites; a plan of the hut to be used should be drawn up and followed. Holes in the ground and borrow-pits should, if practicable, be filled up. Every coolie should be examined, especially as regards enlargement of the spleen, and if found suffering from present or comparatively recent malarial infection he should be isolated; no case with actual enlargement of the spleen should be employed; all persons with a history of recent fever and all infected persons should be given quinine for three months; all cases of existing malarial infection should be isolated in the hospital, which should be at least 200 yards from the coolies' huts. If practicable, immunes only should be selected; the special point to attend to being the exclusion of malaria "carriers." All fresh arrivals should be similarly examined and dealt with. All cases of chronic malarial infection should be eliminated and sent to their homes. During the actual malaria season quinine or mixed cinchona alkaloids in tablets should be issued prophylactically under responsible supervision to all labourers, 5 grains daily or 10 grains on two consecutive days every week, when there is heavy malarial infection or many Anopheles. It is a wise economy to provide all employees with quinine free of charge.

Health statistics—economic and social conditions.—The health statistics of the staff and labour force should be recorded initially, and later on from time to time. These statistics should state: Ages and composition of the labour force; sickness rate, mortality, invaliding rate; chief causes of sickness, invaliding and death; and the records should be so kept up as to show the state of health of the force at a glance. The social and economic conditions require careful attention—wages, food supply, water supply, housing, personal cleanliness, latrines and general sanitation.

Medical inspections of labour force and camp.—There should be a regular medical inspection of the labour force and camp every fortnight, and the spleen rate taken every six weeks or so. A sanitary inspection of the "lines" should be made weekly, preferably daily. The camp must be complete in itself.

A short and explicit set of anti-malarial rules should be drawn up. These should give in the simplest possible language the causes of malaria, explaining its production by parasites in the blood which are introduced by mosquitoes, the way mosquitoes breed, and the use of quinine in preventing malarial fevers. These rules should probibit the creation of borrow-pits and excavations of all

[1] Modified from Carter, *Anti-Malarial Measures for Farm-houses and Plantations*, U.S. Public Health Service, Reports, 1919.

kinds which may become the breeding-grounds of mosquitoes, and direct the covering up of all water stored in the huts. The rules should strictly insist that every case of fever must report sick at once. The class of persons employed is illiterate, and usually of the lowest and most impoverished order of the community. Therefore the anti-malarial rules of the camp should be explained to them by the headmen of the individual gangs.

Europeans and others able to read should be provided with a leaflet of instructions as to how to keep themselves free from malaria. The leaflet should deal briefly and simply with the symptoms, treatment to be adopted, especially the amount of quinine to be taken daily, and the period over which the quinine should be continued to effect a cure.

A certain number of the men should be put on special anti-mosquito duty, their work being much the same as that of mosquito gangs employed in towns and cantonments. Such gangs should be under one of the headmen of the labour gangs, who should be taught the work of a mosquito inspector. He should superintend the work of the mosquito gang and report daily to the officer in charge. These men should be taught their work at the beginning by the sub-assistant surgeon or by the officer in charge. The number of men required will largely depend on the size and nature of the work under construction, the character of the ground, and the area covered. Periodical demonstrations and instruction in anti-malarial measures should be given by the medical officer.

The writer does not advise either screening of huts or the use of mosquito nets for the labourers and their families; they are not sufficiently intelligent to know how to appreciate them or look after them. But for the Europeans and educated and intelligent members of the staff, screening of huts or houses, or the use of mosquito nets, is strongly recommended.

When the work is in a malarious district the site of the camp should never, when possible, be within half a mile of villages or bazaars, or other habitations occupied by the local population. As the work progresses and the camp moves on, the same measures should be enforced in every new site occupied, and no old sites should be quitted until every possible breeding-place for mosquitoes has been abolished.

All such gangs of labourers should be provided with a hospital, no matter of how temporary a nature, with a sub-assistant surgeon or other medical officer in charge, and where there is a number of such gangs in a district a visiting medical officer should see that all anti-malarial measures are being carried out systematically. Amongst such gangs all cases of severe malignant tertian malaria should be sent to their homes if practicable, or arrangements made to send them to an adjacent civil hospital. As with soldiers, so with coolie labourers and all gangs of men under control—when infected by malaria, treatment by quinine for a few days is a mistake, if malaria is to be eradicated. Each infected case improperly treated is a source of constant menace to his companions, and an added factor in the maintenance of malaria through the medium of anophelines.

It is a mistake to send healthy labourers from non-malarious districts to an intensely malarious one. Of men sent in this way a large proportion become saturated with malaria and useless within a few months. As examples of the loss of labour thus brought about are the Gurkha and Sikkim coolies employed on the tea estates in the Duars, etc.[1] When recruiting labour gangs for work in malarious areas, it is advisable to select men from people already immunised by previous attacks of malaria in childhood. The writer has investigated the

[1] This subject has been dealt with in the section on the RÔLE OF MAN IN THE DISTRIBUTION OF MALARIA IN INDIA, p. 45 *et seq.*

malaria of three such collections of labourers, one in connexion with the Bari Doab Canal works in the Hoshiarpur District, another in a large famine relief work, and a third in connexion with the building of a railway extension in Assam, and in each of these there was every condition that could favour the rapid dissemination and intensification of malaria. Much of the malaria produced in these circumstances can be prevented at comparatively little cost. Arguments (chiefly financial) can be brought against some of these suggestions for mitigating malaria in gangs of labourers, but apart from reduction in the dissemination of malaria in India the actual saving in labour would to some extent compensate for the expense.

What has chiefly been relied on in the tea gardens of Assam is *petrolage* of waters in drains, ditches and pools in the neighbourhood of the coolies' huts; killing or driving out adult mosquitoes from the dwellings of coolies infected with malaria; keeping a space round the coolie lines clear of jungle and low vegetation; and filling up of all holes and puddles. The *chowkidars* or watchmen are given tins of kerosene oil, and they are instructed to sprinkle it along the drains at the end of each shower. The oil is carried down by the running water to all the little hollows and inequalities wherever water collects.

In the case of large isolated estates there should, when practicable, be a hospital for all cases of malarial fever, and, where this is not possible, a method for having all hands systematically and regularly inspected; all persons found to be suffering from malarial fever or enlargement of the spleen should be given quinine regularly for three months.

In a labour force, prevalent severe anæmia is in most cases due to ankylostomiasis; thymol, β-naphthol, oil of chenopodium or carbon tetrachloride or other appropriate remedy should be given to all whose dejecta contain eggs of the Indian hookworms. The introduction of a system of conservancy with adequate latrines and incinerators should not be neglected; these conveniences should be as near the "lines" as is compatible with sanitary requirements. Malarial infection complicated with ankylostomiasis is difficult to eradicate.

VI.—Prevention of Malaria in Military Cantonments in India

Anti-malarial committee in cantonments.—Every cantonment now has its anti-malarial committee, whose functions are definitely laid down. They meet once a month, or oftener if necessary, carry out inspections of mosquito-breeding areas, regulate and co-ordinate the work of the various mosquito gangs employed in the cantonment, and in various other ways adopt measures for the control of mosquitoes.

Importance of anti-malarial measures in cantonments.—It is impossible to emphasise too strongly the importance of anti-malarial measures in cantonments in India during peace times. The vast majority of cases of malarial fever occurring on field service are relapses, the initial malarial infection having been acquired in cantonments.

The malaria of cantonments is to a large extent bred in cantonments. Of 3,884 children examined in 1909 in endemic malarious cantonments the writer found an average of 60 per cent. with enlarged spleens, and an endemic index of 40 per cent. Even in European troops' children the spleen index was found to be 32 per cent.

European troops are exposed to malarial infection in various ways—through attacks of anophelines infected by both European and native children, punkah coolies and followers generally; by visiting in the evening bazaars, coffee shops, soldiers' homes and Army Temperance Association rooms; and on "sentry go."

The detection, isolation and specific treatment of infected soldiers are, as in other communicable diseases, of great importance in the prevention of malaria.

Importance of relapses.—At the present time over 63 per cent. of the troops (European and Indian combined) admitted for malaria are relapses (see pp. 13, 14, App. I), due largely to improper treatment of the first infection. In order to prevent them a prolonged course of quinine is required, such as that laid down on pp. 273–277. All troops and followers known to be infected by malaria should be subjected to this course, or some modification of it, for not less than three months. Quinine treatment properly carried out is decidedly efficacious in curbing manifestations of malaria and keeping it within bounds.

In most stations malarial patients are now isolated in special screened wards, or supplied with mosquito curtains; in many instances the whole of the wards in hospitals are made mosquito-proof by wire-gauze doors and windows, and electric fans are used.

Admission into hospital and isolation of cases of malaria.—As just noted, all known cases of malarial fever should be admitted into hospital—they should not be "detained" or allowed "to attend." This is particularly necessary in native regiments, where the men on returning to the lines infect their comrades and frequently get re-infected themselves, there being always, in the malarial season, abundance of malaria-carrying anophelines present and infected native children. The advantage of remaining in hospital is emphasised when, as is now the case in many instances, the hospital is provided with mosquito-proof wire-gauze doors and windows.

All soldiers suffering from known malarial infection should be treated with quinine continuously for at least three months after the last paroxysm. When, as is the case during the malarial season, re-infection is liable to occur, the necessity for such treatment is emphasised. All discharged cases of malaria taking quinine curatively should get their quinine *at the hospital* daily for three months; this enables the medical officer to see the men regularly, and to make reasonably certain that the quinine is really swallowed. A periodical surprise test of the urine will check this.

If the treatment of relapses begins after the malarial season is over a three-months' course is, as a rule, sufficient. The occasional failure of even this lengthy course is no justification for its condemnation. When in any case there is an unusual amount of residual enlargement of the spleen it is advisable that quinine be given curatively for *four* months, no matter what the period of the year is in which it is commenced, and should the end of this course arrive during the malarious season these cases should, like all other men, receive prophylactic quinine.

In malarious stations in many cases European troops during the malarial season may with advantage be removed into camps well away from native towns and bazaars, on the principle of segregation of the healthy (see pp. 216–218). The keeping of European troops in hill stations until the malarial season is over is a measure of considerable advantage.

Prophylactic issue of quinine.—In the present state of our knowledge the writer considers that quinine should be issued prophylactically in endemic malarious areas during the malarial season *if troops do not occupy mosquito-proof barracks.*

When to begin prophylactic issue of quinine.—When all cases of malaria in units are admitted to hospital, and such admissions reach from 2·5 to 3 per cent. of strength, prophylactic issue is justifiable. The longer it is delayed after this the higher will

the percentage of fresh infections become during the malarial season. He would not lay this down as a hard-and-fast rule for adoption. There are circumstances when a prophylactic issue should be made irrespective of the percentage of admissions, *e.g.* on manœuvres at the end of autumn when in a district known to be malarious, or in barracks when there is a sudden rise in the malaria of the civil community around. Assuming a uniform distribution of cases in barracks, any greater percentage than 2·5 or 3 means that one or more men in each barrack room are infected, and that through them, in the presence of anophelines, malaria will rapidly spread by infection acquired in the barracks. In ordinary circumstances such spreading of malaria does not occur through cases in the barrack room of European troops, but through the infected anophelines from married quarters and followers' huts invading barrack rooms. The effect of the percentage of cases of infection in influencing the incidence of malaria may be seen in every endemic malarial district. When the prophylactic issue is postponed until the percentage of cases to strength reaches 5, the effect on the incidence for some weeks will be comparatively insignificant. The men in barracks are then in all probability infecting one another through malaria-bearing anophelines. In such instances the maximum prophylactic doses of quinine should be commenced at once, *viz.* 5 grains daily for 6 days and 15 grains on the 7th day every week, or 15 grains on two consecutive days weekly. The condition of malaria in the civil population is another useful guide as to the time to begin quinine prophylactically. In troops, as a rule, the maximum incidence occurs later than it does in the civil population of the same stations, the number of cases of residual malaria being greater in the latter than in the inhabitants of cantonments. In practically all instances in which they are taken it will be found that the spleen index and endemic index of the civil community in the neighbourhood of cantonments is higher than in cantonments.

Most effective method of using quinine prophylactically.—The writer's experience is that the best prophylactic dose of quinine during the malarial season where malaria is comparatively mild is 5 grains daily—in the evening; where it is severe, 5 grains daily for 6 days and 10 grains on the 7th day; and where it is very severe, 5 grains for 6 days and 15 grains on the 7th day. With these three degrees of malarial intensity it is probable that the results of 10 or 15 grains once a week, 10 grains twice a week, and 15 grains twice a week, in the last two cases on consecutive days, would be slightly inferior to those recommended above. He does not approve of Koch's "long interval prophylaxis" (p. 283), and in stations with severe malaria he considers it dangerous. The great objection raised to the daily use of quinine as a prophylactic to troops is that connected with its administration under responsible supervision. With a little arrangement, however, it may be carried out in regiments without the least trouble. Tablets are much more popular than solution of quinine. The great advantage of the 5-grain dose is that it never has any deleterious effect and never cinchonises.

All children in cantonments with enlargement of the spleen should be given a four-months' course of curative quinine treatment, receiving a dose daily.

Eradication of malaria from children living in cantonments.—In the year 1909, in a special report on malaria in cantonments, the writer recommended that every child with enlargement of the spleen be given quinine curatively for a period of three months. This course may be commenced at any time of year, but it will be more successful during the summer and early autumn. "The object aimed at is to eradicate malaria parasites from these children. This three months' treatment would only be necessary once, for although there would in succeeding years be once more a gradual rise from a low spleen index to a higher, the rate of this rise depending on the assiduity with which cases of malaria occurring in children were treated, the effects would last for some years at least. When the spleen rate in any future year reached 25 per cent., the method, in possibly a more perfected form, could be adopted again. I would here plead for a trial of this under rigid supervision and in a way that will not wound the susceptibilities of the parents."

"The following scheme is proposed, subject to such modifications as local needs necessitate. The drug will have to be taken to the different followers' lines and regimental bazaars and a daily parade of *all* children held. By this means any cases of malarial fever met with would be at once placed on the list of those to get a three-months' course. The parents should not be relied on to administer the drug to children. In the case of European troops' children, the parade for the inspection and the issue of quinine could be carried out at the more central of the married quarters, and should invariably be supervised by a medical officer." [1]

The writer is confident that, if rigidly carried out in its integrity under responsible supervision, the degree of success will be considerable, and that, even if partially carried out, it will effect a reduction of the malarial incidence in troops. It would probably be necessary to repeat this procedure every three, four or five years.

The use of quinine *alone*, curatively and prophylactically, will never eradicate malaria from cantonments; the most that it will do when administered under due supervision in hospital and barracks is to bring about a certain but varying reduction in the incidence of the disease.

Rational hygienic living as an aid to the prophylaxis of malaria.—To maintain good health in malarious stations all precautions as regards personal hygiene must be taken. These are dealt with under PREVENTION OF MALARIA IN THE INDIVIDUAL IN INDIA (p. 304 *et seq.*).

Malaria in the Army in India is usually mild.—In military life in India, except in a few stations, we do not see the more virulent effects of malaria, nor the results of chronic and repeated malarial infection such as one meets in villages in endemic malarial districts, for the simple reason that amongst our troops severe malarial infection is at once brought under treatment, and relapses and re-infections are, to a certain extent at least, kept under control by periodical doses of quinine in cases of known infection, and quinine prophylaxis when general infection threatens. Our troops are better housed, fed, clothed and looked after than the general native community of the country. Further, the malaria of military cantonments is practically always less than that of the neighbouring civil community. Each Indian regiment is allowed to send 15 to 40 per cent. of the men to their homes for several months every year. They are likely to become infected in transit or at their homes. The same holds good with all recruiting parties. The return of these men (except in non-anopheline hill stations, as in the case of Gurkhas in the higher ones) serves to disseminate malaria amongst other men of the corps through anophelines, and, where there are European troops in the station, probably to these also. The obvious remedy here is to allow men to go to their homes only during the non-malarial season and to carry on recruiting during this season also; or to provide them with sufficient quinine to be used prophylactically throughout the period they are on leave or on duty. When quinine is thus provided, full instructions should be given as to how it is to be taken, and, if it is found that it is not used, this should be dealt with as a disciplinary measure. The writer's experience of the use of quinine in this way is that it is very unsatisfactory and only influences the malaria to a small extent. It is better to examine all returning furlough men for malaria and treat with quinine for three months all cases of infection found.

Recruitment of men in endemic malarious districts involves inclusion of carriers, unless they are carefully weeded out by examination of the blood.

Regimental protection.—If regimental officers are fully alive to the great importance of prevention of malarial infection the men will follow their precept and example in carrying out all anti-malarial measures.

Protection between sunset and "last-post" is most essential. That is the time when the majority are infected—the time men are sitting about in verandahs or outside and chatting after their evening games. The wearing of

[1] *Malaria Survey, 7th (Meerut) Division*, 1909, App. II, p. 23.

ordinary "shorts" and remaining in their football clothes, which are saturated with sweat, should be forbidden. "Shorts" that can be turned up at the bottom and buttoned above, and turned down in the evening, are a great improvement on the old kind. The remedies for all these dangers are mosquito-proof (screened) barracks and electric fans or mechanically worked punkahs.

Rest-camp infections.—Many infections occur in rest camps. Such camps are at the foot-hills—Kalsea, Kalka, Dehra Dun, Kathgodam, Jalpaiguri, Metapolium, etc.—all of which are very malarious. Mosquito nets are indispensable in the malaria season in these camps. Screened huts would remove this source of infection.

Measures against Adult Mosquitoes in Cantonments

Mosquito nets and mosquito-proof doors and windows.—Protection against the bites of mosquitoes is one of the most potent ways of decreasing the incidence of malaria. Its efficacy depends upon the standard of anti-mosquito discipline in units, which is largely in the hands of C.O.'s and company commanders. In the case of European soldiers in barracks situated close to native quarters and the breeding-places of anophelines, when these latter places, on account of the expense or for other reasons, cannot be abolished, it is probable that the best method of prevention is that of providing wire-gauze mosquito-proof doors, windows, etc., or mosquito nets for beds (see pp. 299–304). Quinine prophylaxis is unnecessary in screened barracks.

The objection made to mosquito nets is that during the summer nights they are hot and close. This objection may be overcome by allowing the men, after the monsoons have set in and the great summer heat subsided, to sleep in tents, located at least half a mile from any source of malarial infection. This is a compromise to the method of segregation of the healthy from those infected. In most parts of India, as the hottest months are not the most malarious, and the nights are comparatively cool, this objection to mosquito nets does not hold good. To be effective, mosquito nets must be properly employed. This use requires constant supervising by the officers of units. Nets are of delicate fabric and easily rendered useless for want of small repairs. It is desirable that each man should be responsible for the condition of his own net, it being issued to him as an article of kit, and its proper use and care made a matter of discipline. Personal experience shows that soldiers willingly and intelligently use mosquito curtains provided. Many soldiers in different stations buy their own nets; in other stations this purchase is aided by regimental or institute funds. Hence it cannot be stated that heat prevents the use of mosquito nets. Nets are specially necessary for European troops when quartered in forts and other localities in the midst of native towns and cities, where anti-mosquito measures are impracticable, such as the forts in Delhi, Agra, Fatehgarh, Lahore, Ferozepore, etc. In such cases it is also very necessary to change the fort garrison as repeatedly as practicable—once a month at least.

The introduction of mosquito-proof wire-gauze doors and windows for barracks in malarious stations would probably be one of the most economical ways of reducing the admission rate to hospital for malaria of European troops in India. But every detail must be attended to. It is useless to provide automatically-closing wire-gauze doors if they are kept open. At Bareilly in the summer of 1909, when inquiring into the malaria of that station, the writer visited the British station hospital at midnight. It was provided with such doors, but he found all the doors on one side kept open by bricks placed at the bottom, and mosquitoes were "buzzing" in the wards. The hospital was provided with electric fans.

When a long barrack room or hospital ward is screened, there should be only one means of entry on each side—double automatically-closing doors opening outwards.

No matter what form of mechanical protection is provided, the writer would emphasise the necessity of continuing such minor works as can be carried out by mosquito brigades, especially the abolishment of all small breeding-places of mosquitoes, filling up or draining hollows and borrow-pits breeding anophelines, draining off small collections of water, grading ditches and keeping them clear of weeds, oiling pools that cannot be removed, etc. This work should be in the hands of the cantonment committee and superintended by the sanitary officer of the station under the orders of the senior medical officer. Anti-mosquito measures are in many stations regarded as impracticable owing to the difficulties of dealing with rice-fields, irrigation canals and other large masses of water in and around cantonments. In some cases the efforts of cantonment authorities are rendered futile because the breeding-places of mosquitoes are near cantonments and under the jurisdiction of civil municipal commissioners who will not co-operate.

Preventive measures against malaria in cantonments should be independent of the measures adopted by the civil community. In the case of a regiment, company, troop or battery living in quarters located near native bazaars in civil lines, and close to numerous breeding-places of anophelines in such lines, anti-malarial measures, to be successful, must be independently carried out. This is a question affecting the anti-malarial (including the anti-mosquito) measures of almost every large cantonment in India.

Punkahs of one kind or another are used in all European barracks and help to keep off mosquitoes, but they are certainly not a reliable protection against mosquito bites. In many stations in the United Provinces and Punjab such as Meerut, Delhi, Peshawur, Rawalpindi, etc., punkahs are stopped before the end of the anopheline season on account of the cold nights (see p. 24).

Hand-catching of adult mosquitoes.—In barracks, huts, tents and wards of hospitals, adult mosquitoes may be captured in test tubes, in ordinary muslin butterfly nets, in small hand-nets, or in prepared traps. A combination of these will get rid of most of the mosquitoes in barracks and hospitals. Where these places are not screened against mosquitoes, catching may be done daily. Mosquitoes often find their way even into screened rooms. In the malarial season some of the Anopheles entering barrack rooms are almost certainly infected. A few men working in a barrack room or a ward for an hour a day may in the malarial season capture hundreds of mosquitoes. Remember that the mosquito in non-screened barracks and houses constantly makes its exit before the sun rises.

Mosquito Traps.—See pp. 124–126.

Jungle and scrub cutting and burning.—See p. 311.

Culicides, fumigants and culicifuges.—See pp. 306–310.

Mosquito repellants.—See pp. 309, 310. The most commonly used are citronella and Bamber oil. The latter is one of the best applications for those doing guard or other night duties in which they will be exposed to the attacks of Anopheles. Its effects last three or four hours. It should be liberally applied to uncovered parts of the body.

For other measures against adult mosquitoes see pp. 310–312.

MEASURES AGAINST MOSQUITO-BREEDING IN CANTONMENTS

Main anti-larval measures for cantonments.[1]—The chief anti-mosquito

[1] Regarding the subjects of Drainage and Water Supply see section on PREVENTION OF MALARIA IN TOWNS, pp. 365-373.

measures required in cantonments are included in—rough canalisation of streams, irrigation canals and water-courses generally; levelling, grading and embanking of rain-water channels, ditches and roadside drains; filling up of tanks, borrow-pits, excavations and depressions; covering of disused wells; covering, or periodically emptying, or kerosening water cisterns; filling up excavations for bullock runs; kerosening once a week all small collections of water that cannot be abolished; prevention of excavations for building purposes within cantonments; removal of brick factories from cantonment limits; and disuse of grass farms in cantonments when these are near the breeding-grounds of anophelines. Each of the measures enumerated is dealt with under a separate section in detail. The writer would here only refer to a few that appear to be of special importance.

Rough canalisation of streams.—Where streams run through or near cantonments it is possible, by proper embankments and regulation of the bed during the seasons of low water, to lessen considerably the facilities for the breeding of anophelines. The writer is constantly reading in reports that, because a stream or a large irrigation channel is on the confines of a cantonment or town, it is useless to make any effort to reduce anophelines. This policy of allowing things to continue in the old way is one that is responsible for much of the inactivity displayed in regard to anti-mosquito measures.

Irrigation channels.—Where irrigation channels exist in cantonments, as at Peshawur, Kohat, Mardan, and many other places in the Punjab, something can be done by (1) placing automatically-acting droppers containing kerosene at proper intervals; (2) grading and levelling the channel so as to maintain a flow of at least $2\frac{1}{2}$ feet per second; (3) clearing it of all grass and weeds periodically. Algæ, duckweed, etc., may be prevented by a similar automatically acting dropper containing a solution of sulphate of copper (strength 1 pound to 10 gallons of water). Where the cantonment can afford it, these channels should be made *pukka*; where not, then the men operating as a mosquito gang must keep them level, and by rough canalisation and proper grading maintain a uniform flow.

There are cantonments in India, *e.g.* Peshawur, Nowshera, Lahore Cantonment, Jhelum, Amballa, Bareilly, etc., in which properly worked out subsoil drainage schemes of one kind or another would considerably reduce the malaria incidence.

Brick factories.—No brick factory should be allowed within 1,000 yards of cantonments. The building of barracks for Indian troops and followers with *pukka* bricks joined by mortar would do away with the excavations now made to supply mud walls and sun-dried bricks. The initial cost would be greater but the outlay is justified from many points of view.

Rice cultivation.—Rice cultivation should not be carried on within 1,000 yards of cantonments.

Thatch roofs foster mosquitoes.—Thatch should not be used for Indian troops' or Indian followers' barracks. Thatch roofs harbour mosquitoes during the malarious season, and also serve as places in which they may either hibernate or æstivate during the non-breeding seasons, that is, in winter and summer. Tiles are preferable. Mosquitoes cannot stand the heat attained by tiles during the summer. During, and for a time after, the rainy season it is much easier to capture anophelines in a thatch house than in any other.

Borrow-pits.—The creation of borrow-pits or excavating the surface soil for any purpose whatsoever should be strictly prohibited within 1,000 yards of cantonments—the nearer this limit is to a mile the better. The construction of barracks should not be considered completed until every excavation within

1,000 yards created during such construction has been filled up and properly levelled. The writer has found it extremely difficult to prevent the digging of borrow-pits in cantonments, even with the help of the divisional G.O.C., local brigadier and A.C.R.E. The habit in India of using the earth on the spot for building operations is most difficult to oppose successfully. It is the same with any construction work of the kind. The native contractor will not bring the earth from half a mile away.

Grass farms.—These should not be allowed within half a mile of barracks. In several cantonments where cavalry regiments and artillery are quartered grass farms dovetail into the station, are regularly watered by irrigation channels and form breeding-grounds adjacent to the barracks and hospitals. Land springs form, with widespread seepage under cover, a veritable paradise for Anopheles. In the absence of well-planned subsoil drainage or adequate ditching it is difficult to deal with these breeding-places.

Mosquito gangs in cantonments.—The mosquito gangs of cantonments are chiefly employed in kerosening large and small collections of surface water, disused wells, garden cisterns and fire buckets. So treating large bodies of water is a useless waste. The sphere of usefulness of mosquito gangs can be considerably extended. Important parts of their real duties are—filling up small- and medium-sized borrow-pits, holes, excavations and depressions in the ground generally, including the shallower parts of large tanks; removing old pots and pans, broken and discarded chatties, broken bottles, and anything in which water may collect; removing grass and weeds from roadside and other drains and ditches; levelling the beds of large and small *katcha* roadside drains and ditches, and collecting anopheline larvæ.

This duty should be carried out systematically, the labour fairly divided amongst the men, the work regularly supervised by some responsible cantonment authority, such as the cantonment magistrate, cantonment sanitary inspector, sanitary officer, senior medical officer, and other members of the cantonment staff. These officials should be acquainted with all possible breeding-places of anophelines in the station and allot tasks to the mosquito gangs.

Another value of mosquito gangs is that they keep people interested in the work of mosquito reduction in their compounds, and in anti-malarial measures generally. *The success achieved also indicates how readily and inexpensively* anti-mosquito measures on a small scale can be carried out in private bungalows.

In a mosquito gang of three men, one should be provided with a pick, another with a shovel, the third carrying the larvicide used, as well as wide-mouthed bottles for anopheline larvæ, when collecting these latter. These bottles should be ready labelled, and one of the three men should be able to write in the vernacular, noting where the anopheline larvæ were found. The more useful and intelligent of the three should be the headman, who must keep the gang busy and do the same work as the others, himself getting, say, one rupee a month more pay. All larvæ collected should be examined, in large stations by the medical officer in charge of the station laboratory, in small stations by the sanitary officer on duty, or by medical officers of units detailed for malaria work.

Mosquito inspectors.—Each large cantonment should employ a cantonment mosquito inspector for ascertaining the breeding-places of mosquitoes, capturing winged anophelines and supervising the work of mosquito gangs. A staff of such inspectors could be readily created out of junior sub-assistant surgeons and, although expensive, in large cantonments it would be an economical measure in the long run. They would ferret out every breeding-place of anophelines, identify all larvæ caught, capture adult anophelines in native quarters

of cantonments and in the neighbourhood of cantonments, carry out blood examinations, spleen indices, and thus localise the malaria in existence; issue quinine or cinchona febrifuge to infected native children in cantonments and keep registers of these cases. They should be practically conversant with the problems associated with the prevention of malaria. Classes for their training should be arranged during the anopheline season in some large central malarious station. Such training would embrace the identification of the different species of anophelines of India, their larvæ and eggs, methods of capture of winged anophelines, breeding out of anophelines from ova, demonstrations regarding the breeding-places of anophelines, diagnosis of malaria parasites in fresh and stained bloods, methods of staining, the diagnosis of malarial fevers clinically, the action of quinine, the method in which it is used curatively in malarial fevers and prophylactically. The materials for such instruction are to be found in all malarious stations during the malarial season. The course under the Central Malaria Bureau is ideal With the progressive decrease of breeding-places of anophelines in and around cantonments there will be a corresponding reduction in the amount of quinine that will be necessary for curative and prophylactic purposes in garrisons, and the amount of labour required to keep down the number of breeding-places will become yearly less.

In every cantonment printed leaflets should be distributed and placarded in English and the local vernaculars giving a brief and simple account of malaria. The writer has used extensively in barracks the leaflet given in Appendix III.

Anti-malarial leaflets to be placarded in barrack rooms.—See Appendix I.

Many of those **general and special anti-malarial measures** given in various sections of PART III are applicable to military cantonments and should be referred to.

We have dealt with the usual anti-malarial (including anti-mosquito) measures in cantonments. When the civil community and cantonments are conterminous or dovetail into one another, unless corresponding measures are adopted by the former, the full beneficial effects are not likely to be obtained. Unfortunately, also, this makes the anti-malarial work in most garrisons perpetual, as there is a constant infiltration of anopheline vectors from the town, bazaars, villages and civil lines. All barracks immediately adjacent to towns, or dovetailing into towns, should be screened. Where cantonments and the civil community are separated by even a mile, the writer has repeatedly seen Anopheles reduced by 50 per cent. in from one to two years, and in one instance by 70 per cent. in a period of twenty-one months, with a like reduction in the malaria incidence in the troops.[1]

Reduction of anopheline infection.—Infection of anophelines can be largely reduced by systematic clinical and microscopical examination of the blood of the personnel of units and by the segregation and quinine treatment of men suffering from malaria. Such examination is largely carried out, and it is found that during the malarial season 2 to 3 per cent. of British and 5 to 6 per cent. of Indian troops harbour malaria parasites without showing any clinical signs of malarial infection. The microscopical examination of the blood is an arduous task, but from it the origin of mosquito infection in barrack rooms is discovered, and the men are treated before the infection does much harm to their constitution, and before they become regular "carriers" of malaria to others, through anopheline vectors. This measure is applicable to all bodies of men under discipline and control—troops, police, prisoners in jails, inhabitants of lunatic asylums, etc. It is obviously inapplicable to the general civil community.

[1] *Report of the Sanitary Commissioner with the Government of India* for the year 1912.

Prevention of Malaria in Indian Frontier Warfare

All our Indian Frontiers are malarious; the boundaries from Quetta to Peshawur, and the extensive foot-hills of the Himalayas from Peshawur to Burma, are notoriously malarious. Let us assume that a force is operating during the malarial season. In all probability some cases of malarial infection will escape detection during the medical examination as to "fitness for service." The main consideration will be to prevent fresh infections in the healthy.

It is necessary to become familiar with the history of malaria in the areas to be traversed and occupied. There is a great deal of literature on this now in existence which should be consulted. A leaflet should be issued for the information of the troops setting forth the anti-malarial measures to be followed. Medical officers of regiments should give short, practical lectures and demonstrations on malaria. Means of carrying out all the anti-malarial measures ordered should be provided.

Medical inspection of troops and followers before going on field service.—By regulation every regiment must be medically inspected as to its physical fitness before going on service. The medical history of regiments should be examined as regards malaria. All cases of acute and chronic malaria will be eliminated, and all men with a strong malarious history should be rejected, not only on account of their being temporarily "unfit," but because in the presence of anophelines they are a source of infection to others. All followers must also be examined. They are much more likely to be infected than the troops, as many of them live in bazaars. Previous residence in the hills is a point in favour of sending a regiment on a campaign. The writer could quote numerous instances from the records of campaigns in the Indian Empire where the advantages of this were demonstrated.

Campaigns, marches or journeys through malarious districts should, when practicable, be undertaken during the non-malarious months.

A large number of the permanently established camping-grounds on the main roads between stations are located adjacent to native villages, and are therefore, for reasons already stated, sources of infection to troops occupying them during the anopheline season. Most of these camps were fixed upon antecedent to our recognition of the mosquito as the vector of malaria. Camps thus located are convenient as regards water and supplies generally, but there are obvious risks entailed in halting troops in them. Quinine prophylaxis is often required in this circumstance.

Prophylactic issue of quinine on field service.—In military campaigns in India, and on our Indian Frontiers in endemic malarial areas, during the malarious season quinine prophylaxis is the only practical method of keeping a force efficient. The arrangements for the administration of the quinine prophylactically should be properly organised. If the malarious tract covers more than one day's march a prophylactic ration of 5 grains of quinine should be given every evening, beginning after the evening meal of the first day's march. So long as the force continues in the malarious region this prophylactic ration of quinine must be continued. It may, in some very malarious places, be necessary to give 10 grains daily. Tablets are more popular and practicable than mixture.

Fresh infections and relapses.—All fresh cases of infection must be put on a curative course of quinine at once and, if not reacting, sent to the base. Arrangements for anti-relapse treatment should be ensured. The prevention of relapses will usually be found a difficult task. It will, as a rule, be impracticable for military reasons to send all these cases to the base, but decidedly refractory cases must be sent down. It is advisable to carry out what was done on some of the fronts during the War, *viz.* formation of special malaria camps for relapse cases as remote from the body of the troops as the military situation allows. These cases received extra rations, were put on light duty and given graduated route-marches; indulgence in outdoor games was granted, and everything to promote a healthy life encouraged. Definite anti-relapse quinine treatment was carried out. In several instances 15 grains of quinine were given daily for the first ten days, and subsequently 10 grains daily for sixty days, when the course was

considered to be completed. The drug was administered under the strictest medical supervision. When a relapse occurred the patient was taken into hospital and a curative course again given.

In a well-organised, prolonged campaign many of these men (British and Indian) would be sent to malaria convalescent camps or hospitals in non-malarial hill stations, as was done during the Great War.

It is highly important that intensive anti-mosquito measures should be carried out at the bases, and these should, if possible, include screening of huts, barracks, tents, or other forms of accommodation in use.

All swamps and other breeding-places, including wells, and all houses of local inhabitants, should, if possible, be put out of bounds after sunset.

VII.—Prevention of Malaria in Jails, Asylums, etc., in India.

These places are often so situated that it is impracticable to take into account the outside population and their environments, and the work of prevention has to be carried out independently of what is done outside. The population fluctuates almost daily. Breeding-places in the grounds are readily dealt with.

In every case coming into jail the blood should be examined for malaria parasites and the spleen investigated; every case of malarial fever occurring should be isolated in the hospital and thoroughly treated by quinine, thus endeavouring to eradicate malaria parasites from all prisoners. Quinine should be administered to the whole jail population prophylactically during the malarial season.

As with gangs of labourers on construction works, a certain number of the prisoners should be formed into a mosquito gang under a headman; and one or more intelligent men should be taught their duties.

The same rules apply to lunatic asylums, modified, of course, to the conditions of asylum life.

VIII.—Prevention of Malaria in the Individual in India

Personal preventive measures are directed against the parasite in man and against mosquitoes which carry the disease from man to man. The extent to which personal preventive measures will succeed depends to a large extent on whether the person understands their meaning, how far he is in a position to carry them out, and whether he is really anxious to keep himself free of malarial infection. To all grouped bodies of men in India under organised control, instructions are given as a routine measure regarding the cause of malaria and the best way to prevent it—soldiers, policemen, prisoners in jails and similar bodies are taught and the measures advised are to a large extent carried out for them. It is for the civil population that so little is done as regards personal preventive measures by the people themselves, and by municipalities. The last-named should provide the educational part for adults, and Local Governments should insist that such education be imparted in schools.

Prevention of initial infection is usually possible.—This is now admitted. Such immunity may be secured by defences against the bites of mosquitoes and the prophylactic use of quinine during the malarial season.

Individual prevention may be secured by always sleeping under a mosquito net or in a mosquito-proof room; by protecting the body from the attacks of mosquitoes in the evening by proper clothes; by protecting the feet and ankles and legs by the use of proper boots (not shoes) or puttees; protection of the

hands and face is less necessary, as one can always see or hear mosquitoes making for these parts and keep them off.

The mosquito net.—The use of mosquito nets at night, or the dwelling in mosquito-proof rooms, may be looked upon at present as one of the fundamental factors in personal prevention from malarial infection; if either is carried out in its integrity, it secures immunity from such infection even in the most malarious places. Therefore, in unscreened houses, without effective punkahs never sleep except under a good mosquito net.

Disadvantages of the mosquito net.—The disadvantages of the Indian mosquito net are the possibility of its not remaining in position; in the case of a long man the foot may be stuck out, or the arm may be thrust out during the night; or unseen perforations may give access to mosquitoes. One great disadvantage of all netting is that the air within the net gets close and stagnant, rendering sleep in the hot weather difficult. Gauze stuffs generally are somewhat delicate, apt to tear, get foul and have to be washed, and in India often return from the *dhobie* riddled with holes.

The mosquito net is indispensable for travellers, and for sportsmen going into the jungle on shooting excursions in malarious regions. Neglect of its use during the malarial season is always dangerous. In houses not provided with wire-gauze doors and windows it is a *sine qua non*. For further remarks on the mosquito net see Protection from Adult Mosquitoes, pp. 302–304.

Punkahs and electric fans.—Punkahs and electric fans are secondary means of preventing access of mosquitoes to man. Apart from the fact that when a punkah is pulled by hand the man frequently goes to sleep on duty, mosquitoes will often attack exposed parts with the punkah working well. Even when, as is often done, a towel is pinned on to the punkah fringe and its lower edge reaches close to the face, mosquitoes will not be denied their feed of human blood. The punkah puller himself may well be carrying gametocytes. It is safer to have the punkah pulled mechanically. The use of electric or lamp-driven fans in sufficient proximity to the place where the occupant is working or sleeping is an admirable, efficient and comfortable protection against the attack of mosquitoes.

Clothes.—It is when sitting outside in the evening resting after exercise that mosquitoes buzz round and attack the ankles, hand, neck and face. In the latter three situations they are often disturbed at their meal and rarely make much headway. The ankles are a favourite spot and mosquitoes are readily able to penetrate ordinary socks with their proboscides. Even thick socks are not always protective. They seldom penetrate flannel trousers; these should not be turned up, but arranged so as completely to join the shoes or boots and leave no part of the ankle exposed. The clothes worn by European children in the mornings and evenings are decidedly dangerous as regards mosquito attacks, and call for some modification to prevent malarial infection by anophelines. For little boys the ordinary sailor suit answers the purpose if the trouser legs are worn down to the boots. The clothes of little girls also seriously require some modification so as to leave no parts of the legs, ankles or arms exposed. The low-neck evening dress of ladies is decidedly dangerous as it leaves a comparatively large surface exposed for the attacks of anophelines just at the time when the latter are seeking blood. The evening dress should leave as little as possible of the upper part of the body and neck exposed, and it should not be difficult to devise some form of evening dress which would cover these parts with a light material puffed out in such a manner as to prevent mosquitoes reaching the skin through it.

During dinner and at writing-tables at night, mosquitoes congregate beneath the tables in the shade to avoid the artificial light. Hence *it is well to wear* straps below the trousers. With military men at mess (who have the additional advantage of Wellington boots) this is always done, but with mufti evening dress it is very essential. The writer has lived in a place where ladies wore puttees in the evening to protect themselves from the attacks of the thousands of mosquitoes which were always under the table at dinner-time.

Many bites are sustained when wearing "shorts" and when the shirt sleeves are tucked up after work or play. All exposed parts of the body should be protected after sunset.

Anti-mosquito veils.—One of the earliest veils used consisted of a cylinder of mosquito-netting, closed at the top and supported by a collapsible framework, all held in position by tapes. A great improvement on this is the "Mosquinette" (Figs. 107, 108), a form of hood which may be used when going about or lying down. *It is effective and as comfortable as* such a contrivance can be. Another excellent veil, on the same principle, is the "Simpsonette," which was used by our troops during the War in Salonica and elsewhere.

FIG. 107.—"Mosquinette" hood with perforation to permit of drinking or smoking. The fabric of which the net is composed is rendered non-inflammable.

From BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics.*

Anti-mosquito boots.—See p. 306.

Where wire-gauze mosquito-proof doors and windows are not provided in private houses, barracks, hospitals, etc., these buildings should be fumigated with sulphurous acid gas (or other culicidal fumigant) periodically during the anopheline season to kill all adult mosquitoes. The methods of carrying out *fumigation* against mosquitoes are fully dealt with in the section on CULICIDES (p. 306 *et seq.*).

Use of mosquito repellants.—(See p. 309 *et seq.*) In the absence of a mosquito veil apply to the face, neck and ears, and to other exposed parts of the body, Bamber oil or oil of citronella, or solution of Epsom salts (1 ounce to 10 ounces water).

Chills.[1]—Avoid allowing the surface of the body to get chilled. Proper clothing is a potent agency to protect from chills as well as from mosquito bites. This is specially the case in the evening and at night.

Among the common causes of chill is the remaining in wet clothes, whether the result of sweat or of drenching by a heavy shower. The effect of physical strain is well shown in military life when annual training begins in the late autumn and regiments are taken on route marches, carrying their kits; in these circumstances it is not uncommon to find from 5 to 10 per cent. or more

[1] The personal PREDISPOSING CAUSES OF MALARIA are detailed on pp. 34–38.

of the troops in hospital during the first week with malaria, although most of these may seemingly have been free from it during the period preceding the training. A similar experience was common in the early stages of the recent war on the North-West Frontier and in Mesopotamia.

Diet, exercise, etc.—A potent means of preventing malaria is to follow a healthy life as regards food, drink, exercise, bathing, sleep, and avoidance of constipation.

Alcohol.—Alcoholic habits or drinking at all in excess, irregular life, and perpetration of hygienic follies, such as living in insanitary dwellings, all tend to predispose to malarial infection.

In travelling avoid the malarious season if possible.—If the time of the year can be selected for travelling through malarious districts, the non-malarious season should be chosen, and the travelling should be done during the daytime. If malaria is prevalent take 5 grains of quinine nightly. If leaving a malarious district for a non-malarious one, continue the prophylactic dose of quinine for ten to fourteen days after quitting it.

Avoidance of malarious houses.—During the malarial season avoid localities known to be malarious as places of abode, such as proximity to marshes and banks of rivers, and avoid residence adjacent to a native population known to be infected with malaria.

***Dâk* bungalows, etc.**—In India, *dâk* bungalows, rest-houses and circuit bungalows are often in the immediate vicinity of villages or towns. A single night spent in these circumstances in a *dâk* bungalow, etc., may be, and often is, followed by severe malarial fever, if mosquito nets are not used and quinine not taken. In these houses wire-gauze doors and windows are specially indicated.

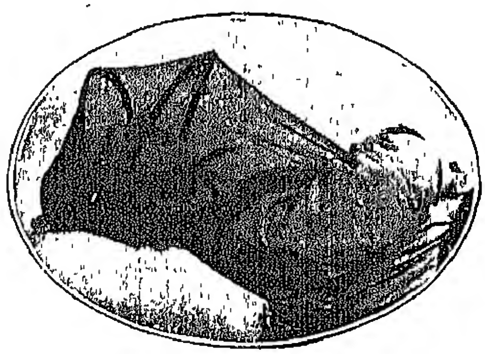

FIG. 108.—"Mosquinetto" hood as worn during sleep.

From BYAM and ARCHIBALD'S *Practice of Medicine in the Tropics.*

In case these precautions are impracticable quinine prophylaxis must be followed—5 grains daily or 10 grains twice a week on two consecutive days, while in endemic malarial areas.

Quinine prophylaxis.—The writer is of opinion that the use of quinine prophylactically is an auxiliary to personal preventive measures; it is specially indicated when the individual is not protected by mosquito nets or mosquito-proof dwellings during the malarious season. It may be taken in any one of the different ways referred to on pp. 283 and 284, which are all applicable to individual protection. The best way is perhaps one dose of 5 grains daily with the evening meal, or on going to bed, supplemented by a 10- instead of a 5-grain dose once a week, say every Sunday evening. In specially malarious localities it is advisable to take 10 grains daily; this may be divided into two doses of 5 grains each. Servants require their daily prophylactic dose of quinine equally with their masters.

The pros and cons of quinine prophylaxis are given on pp. 284 to 290.

After malarial infection has been acquired quinine is the only remedy we possess that will eradicate the parasites. The ordinary prophylactic doses are

then insufficient, curative ones being required. For the curative treatment of malarial fever by quinine see pp. 272–276.

A regular quinine habit during the malarial season is to be encouraged. Those investigating malaria in malarial districts are certain to be infected if the usual precautions are not adopted.

Section 5.—MISCELLANEOUS AND ADMINISTRATIVE PROBLEMS CONNECTED WITH MALARIA IN INDIA

Under this heading it is proposed to deal with:

I. Methods of Measuring the Endemicity of Malaria in India: Malaria Surveys.
II. Education of the Public in Anti-Malaria Measures.
III. Expenditure on, and Limitations of, Anti-Malaria Measures.
IV. Economic and Sociological Problems connected with Malaria in India.

I.—Methods of Measuring the Endemicity of Malaria in India: Malaria Surveys

General remarks.—This section, which deals with malaria surveys and the methods of measuring the endemicity of malaria in districts, towns, cantonments, villages, and in large and small communities, may at first sight seem rather complicated to the uninitiated. In practice it will prove to be otherwise. After a preliminary course of theoretical and practical instruction in the laboratory, there is no method that gives such confidence in the measurement of malaria as a field inquiry under an expert. Facilities for obtaining this field training are now in existence in India and save the beginner much labour and time. On the other hand, it is almost waste of effort for the ordinary medical man who has not had the required preliminary training in malaria to attempt to make a malaria survey and formulate a *practical scheme for an anti-malaria campaign.*

Malaria survey is a convenient term given to an inquiry made in a locality with a view to measuring the amount of malaria in it. We acquire on the spot information regarding the malaria, that will form a basis for practical recommendations for dealing with the disease in the area investigated. It will usually include observations on all the subjects dealt with in this section.

A malaria survey is an indispensable preliminary to serious anti-malarial operations. A complete survey includes:—

A general description of the area—its altitude, configuration, character of soil, and hydrography. The source and storage, if any, of the domestic water supply; whether pools are connected with the source; wells, if any; surface waters—rivers or streams, inundations; any tidal effects; lakes, ponds; drainage, natural and artificial, means of disposal of surface waters; presence of vegetation in water—weeds, grass; agricultural conditions; trees and their distribution; shade afforded by vegetation to mosquitoes; stables, cowsheds and other outhouses offering places of rest and shelter to Anopheles, and in which the insects may be captured; any reclamation of marsh land in progress. Ascertaining whether malaria exists in the area under inquiry; if it does, how it is distributed (spot map) among the population. Past and present history of malaria—whether it is incidental (p. 51), endemic (p. 16), subject to epidemic outbursts (pp. 49–51, App. II), and

if so, to what extent; years of greatest prevalence and extent of prevalence; amount of malaria in existence at the time of inquiry, its seasonal distribution and duration; its effect on the permanent local community, on the susceptible part of the population (non-immunes) and immigrants. A review of all malaria statistics available; case incidence of previous years; areas of special prevalence; conditions of surroundings favouring dissemination, taking into consideration the relation between the local inhabitants and the anopheline carriers. Extent to which quinine is used in the treatment and prevention of malaria, and whether facilities exist for obtaining an adequate supply to meet demands. Population of the locality; general mode of life, social conditions; character, class and grouping of the population; any troops; distribution of the community in town, village, cantonment, etc. Vital statistics—birth- and death-rate per 1,000, infant mortality rate; chief causes of sickness and mortality. Housing conditions—brief account of structure of houses and huts, their sanitary state, lighting, ventilation; density of population on area, overcrowding (if present). Industries and chief occupations of the people—trade, agricultural, etc. General drainage of the country. Local meteorological conditions—rainfall, its effects on the population (p. 21), atmospheric temperature as affecting the local incidence and spread of malaria (p. 19); prevailing winds (p. 22). Facts from any meteorological registers and other local records regarding the climate. Geological conditions and the way they affect the breeding of Anopheles. Means of communication and intercourse with outside areas; inland—roadways, railways, tramways, etc.; maritime and riverain trade—quays, ferries, river crossings, boats, steamers; importation of human and anopheline malaria-carriers in this way. Extent of immigration of infected people from endemic malarious areas, return of permanent inhabitants from pilgrimages and troops from service in malarious regions, immigration of non-immunes (*e.g.* from the hills, Europe); any conditions of non-immune population favouring infection. Method of grouping labouring classes for work. Opening of new industries, new railway towns. Kinds and amount of cultivation, especially rice cultivation, if any; any deforestation; drainage of the soil; floods, drought; irrigation, its nature and extent and effects on the height of the subsoil water. Any other conditions in the physical state of the area or social habits of the people that might affect the local malaria problem.

The following are of special importance: Malaria index and general parasite rate. Spleen index and adult spleen rate. Species of malaria parasites met with in the inhabitants and their relative proportions. Variations (seasonal and other) of local and specific endemicity and causes of these. Human sources of infection and percentage of persons infected to population. Economic, social, domestic and physical conditions of the people so far as these affect the prevalence and dissemination of malaria; recovery rate of malaria; any special points relating to relapses and re-infections; emigration and immigration as they affect the prevalence and perpetuation of local malaria. Numerical prevalence of Anopheles, their species, seasonal and local distribution, localisation of breeding-places. Special investigation as to which are the local natural malaria-carrying Anopheles, and their proportion to other Anopheles. Ascertaining all facts possible regarding the life-history of the local insect malaria-carriers and their bionomics in relation to man harbouring malaria parasites. Sporozoite rate. Hiding-places of adult Anopheles and their places of æstivation and hibernation (if any), hibernation of larval anophelines. Extent to which the population is protected from attacks of adult mosquitoes by wire-gauze screening of houses, huts, barracks, hospitals, by use of mosquito nets, electric fans or punkahs, and

by other means. Any segregation of malaria cases in hospitals or otherwise. Hospital accommodation available for malaria cases.

The survey also embraces house-to-house visits, visits to schools and inspection of school children, and visits to hospitals and inspection of all the area concerned.

In malaria surveys of rural areas and areas occupied by Europeans there are some special points to attend to; these are detailed later.

The length of time taken to make a malaria survey depends upon the purpose for which the survey is undertaken, the extent to which the data enumerated above have been previously and reliably collected and recorded, the size of the area under inquiry and other factors. Assuming that a complete report of the local malaria is required, investigation in a small town or small cantonment, tea plantation or industrial works of any size will take from a week to ten days, in a large town or cantonment from two to three weeks, and in a district probably some months.

A really complete inquiry into the malaria of a district should, however, last at least twelve months, and should show the monthly variations in the factors engaged in maintaining endemic malaria, especially the seasonal variations in the endemic index, number of anophelines (if possible of the malaria vectors) and their sporozoite rate. In any circumstance the scientific and accurate investigation of the malaria of a locality is an arduous and long task. Take the question of the sporozoite rate. In a full inquiry hundreds of several species of Anopheles may have to be dissected—a tedious task, as not more than 100 can be fully dissected and examined in a day. Where anophelines are very numerous, it is possible to go through many hundreds of dissections without finding a single insect with either sporozoites in the salivary glands or zygotes in the stomach walls. Again, the taking of the malaria index of, say, 1,000 children spread over 15 or 20 villages in an area of 25 or 30 miles involves a considerable amount of labour that does not appear on the recorded data. The finding of all breeding-places of anophelines, the collection and specific determination of ova and larvæ discovered, their breeding out, and the carrying out of experimental malaria in the adult females, all form part of a complete malaria inquiry and have their own difficulties. Hence it is that malaria inquiries of a reliable kind in India are very few.

The malaria rate may vary in the same locality within wide limits during different years. Malaria is now only very mild in some of the places where it was formerly severely prevalent, it has increased enormously in certain parts of India where it was previously comparatively trifling; there are localities with sudden fluctuations, and there are others where it is permanently high or permanently low. The endemicity, even in the more pestilential malarial areas, varies very much. The conditions in two places within a few miles of each other may seemingly be the same, yet the malaria index of one is very high, and in the other very low or even at zero. Whilst malaria is universally distributed in India, *it is essentially a local disease*; it is sometimes found to adhere to certain parts of inland towns and cantonments for years, extending beyond these only during epidemic outbursts. In some cases it is at once possible to discover the essential causes of this localisation, in others the inquiry is exceedingly difficult, possibly because they are connected with endemiological and epidemiological conditions regarding malaria that are still unknown. Generally, however, when investigators, after completing their malaria survey, come to review their data, they find that this disparity in most cases is accounted for by the distribution of the breeding-places of Anopheles in the area under investigation. It is necessary, therefore, to ascer-

tain carefully the endemic indices over large areas to get an accurate estimate of the variations in endemic malaria in a district or province. After ascertaining in a general way the chief facts concerning the province, district, town, cantonment or series of villages, we should make a close malaria survey of each area, and every part of each area, to enable us to explain the causes of the variations that will be met with. The malaria rate of any place is not easy to calculate with any degree of accuracy, as there are so many factors which may disturb malaria statistics—accuracy of diagnosis, non-reported cases, cases not treated, cases of infection keeping at work, and so on.

The writer would emphasise that malaria is a local disease; he does so as a counter to those who persist in stating that malaria can never be eradicated from India. In anti-malaria work we do not attempt to deal with India as a whole; we attempt, and in most cases achieve, reduction of malaria in the particular place in which we are operating. The local nature of malaria has recently been stressed in Italy, even to the extent of comparing one story of a house with another.

Lt.-Col. A. G. McKendrick, I.M.S., who has studied the various aspects of the malaria problem from the mathematical side, can find no means of generalising or of correlating the data connected with different malarial areas; the factors are altogether too dissimilar. He states [1] that "the only practical way of investigating malaria is to survey the conditions prevalent in a particular area (such as a town) and forthwith deal with these conditions." There is no short cut.

Staff and equipment required for making a malaria survey.—These will depend on the kind of survey to be undertaken, its scope, objects in view, length of time allotted, and the funds available to meet the expenses. Take a town or a small cantonment. Much valuable information may be acquired by a single expert with a microscope complete with a $\frac{1}{12}$-inch immersion lens, small dissecting microscope, slides, cover-slips, Romanowsky stain, hand entomological net, test-tubes, needles with sharp edges to dissect mosquitoes, small hone and emery paper for sharpening needles, note-books, pencils and other stationery. A trained assistant surgeon or sub-assistant surgeon to catch mosquitoes, collect larvæ, make preliminary examinations of fresh- and stained-blood preparations, help in keeping the records, and be generally useful would facilitate the work.

In the case of a complete malaria survey of, say, the capital city of a province, or a large garrison cantonment, or a whole district, we require two medical men, both trained experts in malaria; one of them should likewise be familiar with entomology so far as mosquitoes are concerned. There are also needed one assistant surgeon and one sub-assistant surgeon, or medical men of their standing, who have been specially trained in malaria. One of these should do the clerical work; both should be able to act as laboratory assistants and help in the field work. If one can drive a car so much the better. The medical man directing the survey should have the power to co-opt the services of an engineer officer, when this is necessary. Four trained orderlies are also required.

Each of the medical officers should have a good microscope with various objective lenses, including a $\frac{1}{12}$-inch oil immersion; the ordinary agents for making microscopical preparations of blood and storing them for future observation; dissecting microscope; photographic camera with telescopic attachment; field binoculars; entomological outfit, including arrangements for collecting and preserving adult mosquitoes, larvæ, ova, etc. (see p. 90 *et seq.*).

[1] *Paludism*, No. 4, March 1912, p. 61.

The stationery, among the usual items, should include paper for maps, charts, graphs and a portable typewriter.

In certain investigations, especially in the districts, a *mobile laboratory* (motor) would be a convenience; it provides a means of carrying men and equipment and enables the medical officers to examine fresh and stained malarial blood at once where they are working, thus saving much time and obviating many of the difficulties in taking back entomological specimens to the permanent laboratory.

The directing officer of the survey may or may not receive specific terms of reference, stating the problem to be worked out, and defining the area concerned, or he may be simply ordered to make a malaria survey of a named district, town, civil station or military cantonment.

Co-operation of local officials in malaria survey.—It is advisable to enlist the sympathies and obtain the co-operation of all who may be able to help in the investigation. It is a useful preliminary to give a few simple addresses and practical demonstrations. The local authorities should have been notified of the inquiry through the official channel, and the director of the survey should have sent forward a *questionnaire* to gather information that can be provided locally. Appendix V—A gives a *questionnaire* which the writer has often employed when investigating malaria in cantonments, towns and districts. It can be readily modified to meet the requirements of any malaria investigation. The form sent out would, of course, have a space for the reply following each question. If local newspapers, English and vernacular, are in circulation, they should be persuaded to publish a notice of the malaria inquiry in hand, explaining its scope and object, and soliciting any local aid that may be required for the investigation. It eases the subsequent work if the medical man in charge of the investigation calls on the Inspector-General of Civil Hospitals, Civil Surgeon, and the local public health and civil authorities; in military life he would call on the G.O.C., S.M.O., and interview the sanitary officer.

Great importance of keeping up a diary.—While it is necessary to fix the programme of the entire survey, so far as this is practicable, before the work is begun, it is also necessary each evening to settle the details of the work for the next day. It is of the greatest importance to maintain a diary of each day's work, as complete as possible; it is a laborious task at the end of a hard day's work, mostly in the sun, but it simply has to be done. It will be most valuable for reference later on, particularly when the survey is finished. Make a weekly summary of the diary. Remember that on completion of the survey a connected report will have to be written dealing with the facts gathered, the general description of the physical features of the area, and how the local malaria is to be dealt with.

Initial general inspection of area under investigation.—Initially it is advisable to make a general inspection of the area to be inquired into, and to grasp the main outstanding features—the densely populated parts, river-banks, low-lying or flooded areas, marshes, and other sites of likely breeding-places of mosquitoes, all in relation to dwellings of the town, or the barracks, or the civil lines; situation of hospitals and so forth. After this the medical man in charge of the investigation draws up a programme of the work to be carried out in consultation with the local authorities; this will require much thought.

Local history of malaria.—In measuring the amount of malaria in a town, district, series of villages, or in a garrisoned cantonment, proceed systematically. Collect information on the previous history of malaria in the locality as ascertained from all locally available statistics, together with the general sickness and mortality rate. Collect literature, maps and plans (old as well as new) of the

area under inquiry. The *Gazetteer of India* series will be found useful, also books of sport, travel, ordinary surveys, reports of railway construction works, etc., of the district or area. There are few districts, towns or cantonments in India that have not had malaria surveys of them made. The malaria officers of provinces have, during the last two decades, collected an enormous amount of information of the most valuable kind, which is all available. Divisional sanitary officers of the Army have similarly reported on the malaria of practically every cantonment in India. The writer has personally made malaria surveys of every cantonment in the Northern Command, North-West Frontier, the old 6th (Poona) and Burma Divisions.

Malaria statistics of a district, town, etc.—In estimating the malaria of a locality inquire into the hospital statistics of malarial cases, including deaths from malaria. Where the diagnosis is completed such statistics may be most useful; usually they are of very little value. The unreliability of most Indian statistics, except those of the Army hospitals, jails, general and municipal hospitals, and those published by the Public Health Commissioner with the Government of India in Simla, is generally admitted. Nevertheless the statistics acquirable in districts give information that would take some time to gather without their aid; they should not be ignored. Therefore, see the medical registers and annual reports kept up in civil hospitals and dispensaries, British and Indian station hospitals, health records of units and industrial establishments, and old and recent health reports, previous and current expenditure on quinine and cinchona febrifuge, not forgetting inquiry of the local chemists, if any. Whenever possible it is advisable to gather one's own statistics in malaria inquiries. The manner of ascertaining the data should be defined and recorded, so that their real value can be estimated by others.

In the estimation of endemic malaria of a locality take into account only *fresh infections*. The large majority of cases occurring in late summer and autumn are fresh infections, whilst those occurring during the spring, early summer and winter are relapses from infections that occurred during the preceding autumn or late summer months; see Tables on pp. 13, 14 and Appendix I with the accompanying remarks. The factor of low temperature in winter is of importance in relapses by reason of its causing chills.

Regarding the individual malaria cases it is necessary to know whether they are indigenous or not. Inquire regarding length of local residence; previous place or places of residence; movements of the family; visits from friends; malarial history of the family recent and remote, and any other particulars that strike the investigator.

The statistical officer of the province may be able to provide valuable data; his co-operation should be solicited. Statistics should be checked as far as possible by local information.

The number of hospital admissions for malaria is not always indicative of the degree of its local prevalence. When the disease is severe and widespread the hospital can only admit a certain proportion of the cases. Here careful scrutiny of the out-patient registers may give useful information. Ascertaining the abodes of the cases of malaria in hospital, and those treated as out-patients, is most useful, for, *inter alia*, it helps in the construction of the spot map.

The amount of malaria having been measured, information should be kept up to date and periodically checked with a view to ascertaining what progress, if any, is being made in controlling the disease. From the data collected in the inquiry a malaria spot map must be prepared. This is a most valuable document for reference.

Malaria map.—Obtain, copy or make an up-to-date map of the area, and

of half a mile beyond it. On it mark all water-courses, wet lands and swamps, ponds, ditches, land subject to overflow, and other possible breeding-places of mosquitoes. Regarding the flat lands, ascertain how long water stands during rainy periods; look for vegetation that is indicative of a high-water table. Mark on the map the ditching, filling in, clearing, regrading of streams and old ditches that is *essential*, and that which will probably be required; this should not be done immediately after rain storms. The *geographical and topographical distribution of malarial diseases* in the area should be noted, together with the varieties of parasites of malaria met with, spleen index and malaria index, and the localisation of adult malaria-carrying anophelines and their breeding-places. Maps drawn to scale should show the points required in distinctive figures, letters or signs. Where the factors regarding which notes are to be made are present, they should be marked with a plus (+) sign, and where

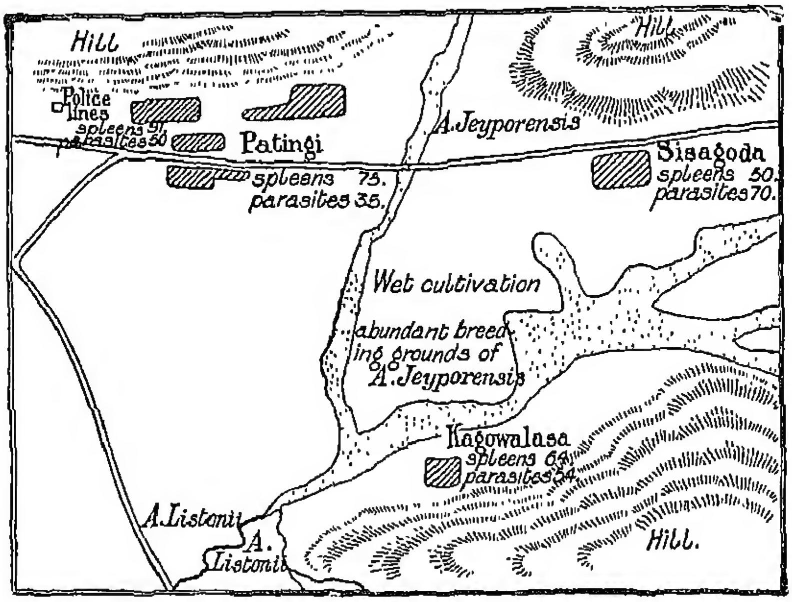

FIG. 109.—Map showing how to make a malaria survey.
From STEPHENS and CHRISTOPHERS'S *Practical Study of Malaria*, 3rd Ed.

absent with a minus (—) sign. Places not investigated should also be marked, otherwise they may be thought to be negative, and erroneous conclusions as to the distribution of malaria arrived at. In ascertaining the incidence of malarial diseases in a town or village, or group of houses, a plan should be drawn and the houses or huts infected indicated in the way described above.

House-to-house visits.—For this a full-sized plan is required for use as a spot map. Select the time of the visits in consultation with the local authorities. Arrange also the times for groups of children and adults to be present at particular parts of the town, cantonment, etc., for medical examination. The times fixed should be those most convenient to the people.

Visits to schools and medical examination of school children.—Arrange the time of the visit with the head schoolmaster. Note the nature of the quarters, surroundings and locality. Examination of roster gives the number of children on the roll; note the number present as compared with

the roster, and their general condition. Examine them class by class. Note any children with malaria, their ages, and homes. Make blood films; ascertain whether they are taking quinine or cinchona febrifuge, if so, mark "Q" on slide with grease pencil. Examine all for enlargement of spleen; presence or absence of kala-azar to be noted. Note any cases of chronic malaria; presence or absence of anophelines in the school; breeding-places of mosquitoes in and near the school. A few handfuls of coppers scattered among the pupils form a useful ally.

It is necessary now to indicate the purpose served by the different items of information collected, and to attempt to estimate the value of each in reporting on the local malaria.

Prevalence and distribution of malaria.—Ascertain the *endemic index of malaria* whenever possible and the *spleen index*.

Endemic index of malaria—meaning of.—STEPHENS and CHRISTOPHERS have shown that the number of native children with malaria parasites in their blood is the best estimate of the malarial intensity of a place; and from this they evolved their now well-known *endemic index of malaria*, or the percentage of children up to ten years of age with malaria parasites in the peripheral circulation. To be reliable, of course, the numbers examined should be large—with small numbers the probable error may be so great as considerably to lessen the intrinsic value of the figures. If time is available enter in a register the names of the persons whose blood is taken.

The accuracy of the endemic index will depend on the degree of care and length of time given to the examination of the blood. In this a time limit is fixed or examination of a certain number of fields is relied on, always examining the edges for choice. It is certain that either way a small percentage of infections will be missed, but the error from this is small. Where it is possible a second, and even a third, examination of negative cases is advised; *e.g.* G. Macdonald,[1] in 1926, in Freetown (Sierra Leone) examined 49 children. The first examination gave 47 per cent. positive as regards malaria parasites; in 6 subsequent examinations there were 86 per cent. positive. In another group of 37 children the first examination gave 40 per cent. positive; 6 later examinations of these 37 raised the percentage to 84. It may save time and give more reliable results to work out the degree of error due to one's own personal equation. In all published records the thick film adds considerably to the numbers of positives, but its use implies that the worker is thoroughly familiar with malaria parasites—failures are many in thick as well as in thin films.

It is doubtful which is better, a time limit or going over a certain number of fields; the former will suit some observers, the latter others. If a time limit is adopted, perhaps ten minutes is required for a thin film. In this period about 200 fields of a $\frac{1}{12}$-inch oil immersion lens can be gone over. An examination of 200 fields is advised. If it is merely a question of diagnosing malaria and parasites are numerous, ten seconds and a few fields suffice. Parasites are usually more numerous along the edges of the film and decrease in number towards the centre.

Details of the examination.—Having decided on the locality to be investigated, a village, part of a town, a *bustee* or a series of *kinthals*, get the assistance of officials. Have a muster of the children made. Do a spleen test first, as this gives no bother and will assist in taking the blood films subsequently. Take a few films of adults and older boys as a preliminary to those of the younger children. The little operation should be carried out with the least possible fuss. A single smear from each is usually sufficient. If the

[1] *Ann. Trop. Med. and Parasit.*, 1926, p. 255.

area is but slightly malarious two blood films may be made from each child, and this should be done if there is likelihood that a differential count will be made. The more taken, the greater will be the accuracy of the test. Trouble in connexion with the endemic index of bazaars or villages is practically never experienced. A small feast of bazaar confectionery at the end of the process, or a copper for each child, removes all difficulties.

Prepare a large number of slides; place them in a slide box which an assistant carries. Keep the slides removed from the box reversed on account of dust, and immediately after making a film place the slide in the rack on account of flies. Make moderately large films, and *examine the first drop*; it may contain five or six times more parasites than the second; do not wipe away the first drop, as the books say. A fair-sized film also allows of a differential count of white cells if necessary. Using a needle or pencil, mark each slide, on the blood film, with a number corresponding with that on the index card or in the note-book; in the latter enter any special points to be investigated in particular cases. Arrange for fresh preparations to be examined at once if this is considered necessary—despatch them to the laboratory; this is easy when two medical officers are working on the inquiry or when there is one good trained assistant. With a travelling laboratory motor-car, examination can be done on the spot.

How to study the blood films collected.—Stain all the thin films with Leishman. Record in each case the number of parasites in 200 fields, type of parasite, result of a search for pigmented leucocytes; if there is time, percentage of white cells determined on a count of at least 500 cells, examining chiefly along the edges. *Do not examine first drops in differential counts* (see footnote, p. 142). If there are no pigmented leucocytes a differential count is perhaps of doubtful value. Note whether gametes are present and whether male or female. It is said to save time to work with thick films stained in blocks of twenty-five each (p. 147). Some experts use the thick-film method exclusively in field work. The author has never been satisfied with the results obtained with thick films, and was never able to rely upon them, perhaps because he was not sufficiently expert with their use.

Age-groups of children in endemic indices.—In taking an endemic index it is necessary to take age-groups, and the actual number of slide preparations of blood of each child should be recorded. In some places the endemic index may approach 100 per cent. At the village of Maram in Manipur, in the month of December 1904, when taking the endemic index of the place, the writer found that, of 72 children between 0 and 10 years of age, 70 had malaria parasites in their blood. In most malarious districts it will be from 25 to 50 or 60 per cent. in the malarious season. The endemic index varies with the age of the child. It is highest between 1 and 2 years, decreases between 3 and 10, and is lowest after 12 years. When making comparisons of the endemic index of localities, this age incidence is an essential factor, considering the probable disparity and rapid decrease in numbers of children affected by malaria parasites after ten years of age. It is, therefore, important that, in comparing one district or village with another, the figures for comparison should be in age-groups. "By investigating the blood of children in this way remarkable variations in malarial endemicity are found, and it is the easiest and best way of getting a true idea of the intensity of malaria in any place. Further, the monthly variations in malarial intensity can be readily followed by this method, and we have in it a simple and satisfactory way of estimating whether anti-malarial measures have had any effect whatsoever" (STEPHENS and CHRISTOPHERS).

An enlarged spleen does not necessarily mean present malarial infection—it is usually the result of an antecedent infection; in all probability, however, parasites are present somewhere in the body, if not in the peripheral blood. It is not often that malaria parasites are found with a chronically enlarged spleen in the absence of re-infection. In 101 cases of enlarged spleen met with on the hills due to antecedent infection the endemic index was about 10 per cent.

Wherever it can be carried out, the writer would recommend a combined investigation of the endemic index, spleen index, general spleen index and general parasite rate. Were these carried out in sufficiently large numbers in various districts and their relative percentages estimated, we would eventually be able to determine the actual malarial intensity of a locality from the percentage of cases of enlarged spleen alone, and enlargement of the spleen is a physical condition that can be diagnosed easily.

Spleen index.—The *spleen index* may be defined as the percentage of native children between 0 and 10 years of age with malarial enlargement of the spleen. It should not, in India at least, be limited to children between 2 and 10; 32 per cent. of children between 0 and 2 years suffer from enlargement of the spleen in ordinary endemic malarial districts. Remember that the normal spleen is palpable in from 1 to 2 per cent. of children in non-malarious places, so that mere feeling the spleen under the left costal arch does not necessarily mean malarial enlargement. Regarding the spleen and endemic indices of village school children, it is well to remember that the scholars often come from two or more widely separated areas, and unless the addresses are taken, the statistics are likely to be a jumble with no meaning.

In some investigations the author has found every child up to five years of age with enlarged spleen. In October, 1900, all the children in the Native Infantry Lines, Daryagunj, Delhi, had splenomegaly.

DANIELS[1] says: "A large proportion of enlarged spleens between 2 and 5 years of age is an indication of a high endemic index," and is then often coexistent with current malarial infection in the spleen cases. M. A. BARBER states: "The spleen index appears to afford a very sensitive, accurate and easily applied method of detecting present or recently acquired malaria."[2]

In their investigations on children with splenic enlargement and the presence of malaria parasites in their blood STEPHENS and CHRISTOPHERS found:

"(1) In the early ages, 1 and 2 years, the number showing parasites is usually in excess of those showing splenic enlargement;

"(2) Above 2 years the spleen rate is usually somewhat in excess of the parasite rate:

"(3) Above 10 years the spleen rate is usually considerably in excess of the parasite rate."[3]

With an unusually high endemic index in children and with endemic malaria constant, the children above the age of ten years show conspicuous immunity. In places where the endemicity is less intense and subject to marked abatements or intermissions, the immunity is correspondingly less obvious, and the parasite rate in adults may be distinctly higher than in more malarious places. The endemic index of children in endemic areas will usually be higher than that of the population in general. When the parasite rate in the population as a whole is very high, say 70 to 80, it is moderately safe to assume that practically all persons are infected; exceptionally this may not be so.

[1] *Tropical Medicine and Hygiene*, Vol. I, pp. 82, 83.
[2] *Trop. Dis. Bull.*, 1921, p. 507.
[3] *Practical Study of Malaria*, 3rd Ed., p. 212.

The *general spleen rate* is the percentage of the entire population with enlargement of the spleen. The writer would here advocate for *general* adoption the use of the *spleen census*, instead of the endemic index and parasite rate, as a means of giving a fairly accurate estimate of the amount of malaria. As far as rural malaria is concerned, the village headman is quite capable of diagnosing enlargement of the spleen, and he could be entrusted with keeping up for each year a register of the general spleen rate (the spleen enlargements in all ages of his village community) and that of children between 0 and 10 years. Enlarged spleen *may* indicate only a past infection, but in practice this really works out to an *actual* infection.

It is conceivable that were sufficiently extensive observations on the general parasite rate, endemic malarial index, general spleen rate and spleen rate of children made, with the ratios existing between these in the same districts, we could eventually formulate from these the actual malaria rate from the spleen rate. These original observations would necessarily have to be accurate in every detail. The relation between the spleen rate and the parasite rate is a complex matter which has been worked at by some of our greatest malaria experts; but it is not as yet possible to formulate the relationship.

Ascertain the spleen rate in as many groups of houses and schools as possible, noting the proportionate prevalence of different degrees of enlargement, and enlargements according to age-groups.

The spleen test is a valuable aid to an inquiry when the age and race are also recorded. In general terms it may be said that, when cases do not run into malarial cachexia, the spleen does not continue to enlarge, once some degree of immunity is established. The test is easy to carry out, and a large number of people can be examined in a short space of time. If we can exclude kala-azar in the locality under inquiry, the spleen index is most useful. In extensive inquiries which have to be carried out in a short space of time, it is the best test of local malaria we can obtain. Malarial splenomegaly indicates previous, not recent, infection.

Age of individuals examined.—Certain *precautions are necessary in employing the general spleen rate* to indicate the endemicity of malaria. Enlargement of the spleen from malaria usually disappears when the patient is no longer liable to malarial infection. In many malarious places the adult population is but little affected with splenic enlargement. In localities where kala-azar or other causes of splenomegaly exist, the spleen test has to be used with caution. In regions where endemic malaria is of medium intensity, or even mild, and this embraces a large part of the malaria in India, spleen enlargement is met with in the adult population to a varying extent.

Significance of the spleen rate.—It gives the percentage of children whose spleens can be felt by the ordinary rough manipulation practised in the field. It is more reliable as indicating the average prevalence of malaria than the actual malaria incidence at the time of the observation. A periodical spleen census is easily carried out by medical subordinates. The spleen rate determines the localities that are mostly affected, it gives us some guide as to the effects of anti-malarial measures, and it marks the people, especially children, who require quinine treatment. Another advantage of the spleen index is that it is not affected by meteorological changes, as is the case with blood examinations; a sudden lowering of the atmospheric temperature or a shower of rain may light up relapses in dormant malarial infections.

As above stated, it is always necessary to make sure that kala-azar is not endemic in the district. The few cases of splenomegaly arising from leucocythæmia, Banti's disease and other causes are so rare that they may be neglected

in estimating general statistics of the malaria of India. A form of Banti's disease has been considered to be one of the ultimate effects of prolonged malarial infection.[1]

The endemic index shows current infection. It is valuable in giving us reliable information regarding local and seasonal changes in the intensity of malaria. The spleen rate indicates the general result of malarial infection during the malarious season; enlargement of the spleen, when untreated, continues for the greater part of the year, and the spleen index may be taken at any time. During the non-malarious season, especially in the late summer and before the monsoons commence, the parasite rate in children in malarious places may be very low, but the spleen index, although at this time at its lowest, is in such places always fairly high. In cases of splenomegaly during the non-malarious season the parasite rate is as a rule low, parasites being then usually only found during the actual relapses.

In taking spleen rates we must have a rapid method of making the observation. The writer has at times dealt with over 1,000 enlarged spleens in children in a week. The great advantage of the spleen index over the endemic index is the fact that it takes only a few seconds to examine and to learn the particulars of each case, whereas blood examination takes at least a few minutes, excluding the time occupied in staining, which may be done by an assistant. On one occasion he examined 264 children for spleen enlargement in 67 minutes, and during this time noted the presence or absence of fever, anæmia, whether the enlargement dated from the preceding year, age, existence or not of chronic malaria or malarial cachexia, and often the exact group of huts in which the children lived. The method adopted was to arrange the children in a row. An assistant wrote in a note-book the headings—name of station, bazaar or group of huts, etc. Then the children as they passed along bared the upper part of the abdomen, the writer palpated and called out the age, whether there was enlargement of the spleen or not. Suppose the child were six years old, had an enlarged soft spleen and anæmia, he called out "6—1 A," if the spleen was large, hard and resistant, he said "6—1 × (cross)." In this way the youthful population of a large village can be dealt with expeditiously.

In children the percentage of positive blood examinations is usually less than the spleen index; in the same groups of children the *average* endemic index in 600 blood examinations was 40 per cent., the average spleen index in 3,884 children was 60 per cent. There was no kala-azar in the stations in which observations on these 3,884 cases of splenomegaly were made, and in only one instance was the enlargement non-malarial. It is not included. The parasite rate in 250 unselected cases of enlargement of the spleen (125 adults, 125 children from 3 months to 10 years) during the malarial season on the plains was only 24 per cent.; 203 of these cases had suffered from periodic fever during the previous two or three months, and five had fever when the observations were made.

The spleen index rises about six weeks after the commencement of the rains; the endemic index at this time does so much more rapidly.

The proportion of malignant tertian parasites found in cases of enlarged spleen in children is considerably higher than that met with in adults suffering from malarial fever in the same localities; for example, the benign tertian percentage for native troops was 88 and the malignant tertian 12, as compared with 65 and 35 respectively in all children up to 10 years of age. The writer is unable to explain the reason for this fact, although its solution is of some importance in the epidemiology and endemiology of malaria.

[1] The subject of kala-azar is referred to on pp. 204, 205.

In spleen cases of children there is a higher proportion of malignant infections (as indicated by "crescents" or "malignant tertian rings") than in non-spleen cases. Of 281 children with enlarged spleens malignant tertian parasites were found in 19 or 6·8 per cent., and benign tertian parasites in 13 or 4·6 per cent. Of 240 children without enlargement of the spleen malignant tertian parasites were found in 8 or 3·3 per cent., and benign tertian in 80 or 33·3 per cent. Except when the child was actually suffering from a paroxysm, the number of parasites in all cases in the individual blood films (with or without enlargement of the spleen) was small; this was not invariable. The parasite rate up to 2 years of age was comparatively high; it ranged from 20 to 68 per cent. in different plains stations. From 3 to 5 years of age it was 19 to 37, and from 5 to 10 years of age 11 to 21.

The amount of malaria transmitted from children with enlarged spleens may vary in different districts, towns and cantonments and is related to the speed of recovery, number of relapses and other factors, some of which are unknown.

In places where there is a constantly high endemic index the spleen rate is as true a test of the measure of malaria as the endemic index itself, except in instances where a previously healthy locality has suddenly become malarious, or when a previously endemic area suddenly becomes an epidemic one. To give the most reliable results it is necessary that the spleen index be limited to the same age as the endemic index, *viz.* 0 to 10 years, and that there be a moderate degree of uniformity in numbers in the distribution of the age-groups of children.

There is a considerable but undetermined amount of residual malaria in children, as shown by the fact that in places of high endemicity 60 to 80 per cent. of the cases of malarial fever are relapses from the preceding year's infections. All cases of enlarged spleen that continue from one year to the next are maintained by relapses which may occur at all times of the year, or by re-infections during the next malarious season; usually both these conditions co-operate. Over 97 per cent. of malarial enlargements of the spleen in children would disappear spontaneously within a year (often within a few months) without such relapses or re-infections.

On examination of 987 spleens of native children at various hill stations in the 7th (Meerut) Division, the enlargement of the spleen had disappeared spontaneously in twelve months. There were throughout the writer's inquiry only three exceptions to this; in two the spleen was 3 inches below the left costal arch, and in the other only barely palpable. In all three the spleens were decidedly hard and probably fibrosed. The important inference from this is that in plains stations enlargement of the spleen is maintained by re-infections or relapses, or both combined, and that if these can be prevented the enlargement will disappear within a year, and malaria parasites will probably vanish from the blood. This enlargement in children shows that the infection is continuous and repeated from one year's end to the other. The spleen index, as shown in native children from 0 to 10 years, is a reliable measurement of the amount of malaria in most places in India, whether it be a group of huts, a bazaar, cantonments, or a town, so long as the numbers are sufficient to exclude a high degree of probable error. The writer ascertained that where the spleen rate is very high, that is over 65 per cent., the percentage of cases of spleen enlargement, extent of the enlargement, and the number of cases of chronic malaria and malarial cachexia met with in children, bear a close relationship to the proximity of breeding-places of anophelines.

The spleen index of European soldiers' children cannot be taken as a

measure of the malaria of cantonments. These children have in many cases been to the hills for part of the summer or autumn, or both, and a large number have had quinine whenever paroxysms of malarial fever occurred. European children are better fed, housed and cared for generally. Nevertheless the amount of malaria in European soldiers' children is an important factor in the malaria of cantonments. In the autumn of 1909 over 32 per cent. of these children had enlarged spleens, notwithstanding that over 35 per cent. of them had been in the hills during part of the summer. The spleen index attains its maximum value as an index of malaria in the children of native villages who get quinine neither curatively nor prophylactically.

The writer on several occasions had his attention directed to breeding-places of Anopheles by finding a high splenic index in particular quarters of cantonments or bazaars; wherever the spleen index is high the breeding-places are not far off. If the children of an endemic malarial town are examined according to streets, or in relation to streams, irrigation channels, ponds or swamps, it will often be found that the percentage of enlarged spleens may vary from 60 to 5. DARLING (1923) arranged the children of a Brazilian village according to the streets from which they came, and found in those from two rows of houses nearest the river a splenic index of 74, from the next five rows one of 26, from the next four one of 4, while beyond that it was 0. The index pointed straight to the river-bank, and there anopheline breeding-places were found and dealt with.

Ascertaining the spleen rate is incomparably the most practicable method of determining the prevalence of malaria. It is easily carried out, can be readily checked, and is delicate and reliable. Determining the parasite rate is not practicable in dealing with the population of a large district, and even in a town or cantonment involves altogether too much labour. Nor does it present any great advantage over the spleen rate.

S. R. CHRISTOPHERS,[1] speaking of the splenic index, said: "The ease with which it can be ascertained over large areas and for large numbers makes it a unique index in the measurement of disease, and to the malariologist it is one of the most precious assets of his science." The writer would emphasise this because attempts have been made to depreciate its value. Few malariologists have examined more spleens than himself; he has, therefore, some grounds for his opinion as to the high value of the spleen rate. Sir PATRICK MANSON a generation ago said that "what is found in the peripheral blood in malaria represents only an overflow from much greater visceral happenings. The splenic enlargement is one result of such happenings and is as important a measure of the malaria incidence as the microscopical examination of one thin film of blood." In areas subject to severe epidemic outbreaks of malaria the splenic rate is a less fluctuating index of the malarial potentialities than the endemic index, and is, therefore, more reliable.

The employment of the *general* spleen rate as an index of the endemicity of malaria is not new in India; long before Laveran's discovery it was used by various committees for this purpose. In September, 1845, the Government appointed a Committee, with Colonel BAKER, R.E., as President, and Surg.-Maj. D. DEMPSTER, I.M.S., and Lieutenant YULE, R.E., as members, to report on the causes of the unhealthiness which existed at Kurnaul and other portions of the country along the line of the Western Jumna Canal, and whether any injurious effect would be likely to be produced on the health of the people of the Doab by the then contemplated Ganges Canal. In 1847 the Committee submitted their report. The endeavour of the Committee was to ascertain what

[1] *Trans. Fourth Congress Far Eastern Assoc. of Trop. Med.*, 1921, Vol. I.

relation existed between certain physical conditions of different districts and the liability of the inhabitants to malarial fevers. At the beginning of their inquiries they experienced much difficulty in obtaining reliable testimony on the latter point. In this difficulty Dr. DEMPSTER suggested that the condition of the spleen in any number of individuals would be a fair test of the probable extent to which they had suffered from malaria. This suggestion the Committee adopted, and thus was established the test, long known as "DEMPSTER's test," which has been used in so many subsequent inquiries of a nature similar to that which engaged Colonel BAKER's Committee.[1] Dr. DEMPSTER wrote :—"I have no wish to exaggerate the value of the spleen test. There may be different types of malaria, giving rise to different complications and consequences, but from what I have lately witnessed, I am fully persuaded that it will be found a true and faithful comparative measure of marsh malaria in its extended sense."

One great defect of the *general* spleen test is that some cases of present malarial infection in adults do not show splenomegaly. "The conditions that lead to splenic enlargement after malarial infection vary and are not thoroughly understood" (DANIELS).

The writer has dealt with the subject of the *Spleen Index* and *Spleen Rate* at some length, as he is firmly of opinion that one or other of these is the only practicable method of gauging the malaria of India on a large scale, and also because he is convinced that it fairly accurately indicates the incidence of malaria in a locality.

An absolutely correct estimate of the amount of malaria in a locality would necessitate the examination of the blood of every person in the locality; not necessarily on one occasion only. This is impossible in a large area. It would also necessitate similar examination in the case of all immigrants. We would then have two groups—the *imported cases* and those that are indigenous, and "the ratio of the numbers of each class to the total population might be called the *infected malaria rate* and the *indigenous malaria rate* respectively" (RONALD ROSS). In military cantonments the number of imported malaria cases may be very great, and the same holds good for some hill stations.

The number of cases of malaria in a place in a given time to a considerable extent depends on the number of infected anophelines, and this latter on the number of anophelines that have bitten infected persons. The former could be calculated if we could estimate the latter. Ross states : "In a village in which there are 1,250 people, 750 infected persons and 30,000 anophelines, the malaria rate is 0·6, the number of anophelines to each person is 24, the monthly infection rate per cent. is 0·72. That is, if a person lives in the village for a month his chances of becoming infected will be as 72 to 10,000," and he works this out by an elaborate mathematical formula which need not be here further referred to. When a place is very malarious at particular periods of the year the infection rate is very high at such periods. There may be comparatively little malaria at other seasons. Once a high endemic index or spleen rate is established in a locality, a comparatively small malaria-bearing anopheline population is capable of maintaining a high endemicity. There are stations in which a small neglected stream, a few tanks or collections of water keep up the anophelines from year to year. In the same way an area with a high degree of endemicity, so long as cases of malarial infection remain untreated, continues to be endemically malarial for some time after the breeding-grounds of anophelines have been abolished, probably because some anophelines immigrate to maintain the malaria, or possibly because some unnoticed source of anophelines, such as

[1] F. N. MACNAMARA, *Climate and Medical Topography of British India*, p. 371.

a disused well, remains. Such may be the explanation of the seeming failure of some anti-mosquito measures. This indicates the necessity for combining both anti-mosquito and anti-malarial measures—removing breeding-grounds of anophelines and treating all cases of malaria with quinine for a period of three months.

Romanowsky stain.—Rapid and reliable work can be done with good dried blood films stained with a Romanowsky stain. The form of Romanowsky preferred is Leishman's carried in crystals or "Soloids" and made up fresh (see pp. 144, 145). Note the number and percentage of films showing parasites or pigmented leucocytes, and the percentage of each species of Plasmodium, if there is a sufficient number to make this a useful record. Where there is no hurry and the examination can be carried out within a few hours, it is always preferable to go over one fresh and one stained slide. When a large number of cases have to be investigated in a limited time, as usually happens in an inquiry into the malarial endemicity of a locality, stained slides are preferable for many reasons. Fresh films should be examined as soon as possible, but when "ringed" with vaseline they will keep many hours. Usually a few minutes' examination suffices for diagnostic purposes, although it may take half an hour to grasp all the peculiarities of some slides. When there is available a sufficient number of trained assistants the *thick-film method* (pp. 146, 147) may be adopted; it ensures greater accuracy in the endemic index. In the writer's hands it has been only a useful accessory; it takes up too much time for general employment in survey work in the absence of much technical help. If, however, BARBER and KOMP's method of staining thick films in blocks of twenty-five is adopted (p. 147), it will replace the ordinary stained thin film and save much time. Each thick-film slide has at one end of it a thin film, which is only stained when some special point requires clearing up. The writer has no personal experience of this method.

Parasite rate.—The *parasite rate* is the proportion of persons of all ages harbouring malaria parasites in the blood. It must necessarily be limited to small numbers of people in a town or district, so that it is most useful in small communities or small bodies of men such as troops in garrisons, prisoners in jails, etc. It is impracticable on a very large scale. Hence when an extensive inquiry is undertaken we are obliged to go by averages taken from a limited number of blood examinations. Usually, during the breeding season of Anopheles, a very high parasite index (60 per cent. or more) will be associated with a high anopheline rate, but a low parasite rate is not necessarily associated with a low anopheline rate. A parasite rate of 25 per cent. may occasionally be met with when anophelines are so scarce as to be difficult to find.

Percentage value of leucocytes.—The most noteworthy change in the leucocytes in malarial infection is an increased percentage of large mononuclears, so that at times they may be equal to the polymorphonuclears. This is specially the case during the apyrexial period of malarial fevers, when there is a leucopenia. "If from any cause a leucocytosis is present the increase of large mononuclears may not be evident." Anything above 15 per cent. of mononuclears is valuable as an aid to diagnosis in the absence of parasites. When large mononuclears are characteristically present, they are to be found in every field and some of them may be pigmented. When scanty a careful differential count *over several slides* may be necessary. A differential count of leucocytes is specially useful in cases where quinine has been taken, where diagnosis is uncertain, or where enteric or other infective fever is suspected.[1]

[1] At least four different kinds of mononuclear cells are described in the blood, and the question of their relationship to malaria requires revision and more precise definition.

Care of slides and records.—When there is a great number of slides for examination, each should be numbered and dated at one end, and the note-book carried should contain all the other particulars of the case, each case having, of course, a number corresponding with that on the slide. Grease or wax pencils are invaluable for quick work in marking slides, and a supply of these pencils should be at hand.

Survey of breeding-places.—"Prepare copies of sectional maps of area to be surveyed for use in the field and for use in the laboratory. Inspect completely every part of the areas of waste land, cultivable land, gardens, depressions, lie of the land for drainage and existing drains, subsoil-water level at different spots. Map in the actual collections of water by means of continuous lines, depressions with drying-up collections, and areas with high subsoil water (indicated by patches of *green* grass, or ascertained by actual digging). Include holes in trees, natural receptacles of plants, investigate crowns of cocoanut, date and areca palms, if there are any. Show on the map where larvæ are actually found, that is the present breeding-place, within an area, say, of 200 to 400 yards' radius, and any areas likely to be breeding-places under favourable circumstances. If no larvæ are found in the latter, this should be marked on the map. Make large crosses to indicate that larvæ are abundant, small ones when they are scanty, and 0 when absent. From each actual breeding-place take labelled specimens, noting the breeding-place; ascertain the common species, and those in fewer numbers. Of the collections of larvæ found, some are to be examined, others bred out to check identification.

"Now go wider afield and ascertain which are the less obvious breeding-places of Anopheles connected with the inhabited areas under inquiry. Note the collections of domestic water actually containing larvæ, and those that are potential breeding-places. Examine uncovered cisterns, chatties, waste water of stand-pipes, hydrants, taps, irrigation wells, etc. Examine wells by means of a hoop net and rope, state the result as regards Anopheles and Culex larvæ. When these observations are completed, enter them on the laboratory copy of the map, which must be absolutely correct in every detail that relates to the breeding-places of Anopheles. It is a permanent document of the utmost importance for all future reference."[1] In the case of each breeding-place note at once—its nature, extent, source of the water, use, etc., and the best way of dealing with it. Note, too, all ground liable to be flooded in the wet season. Make likewise sketch plans showing breeding-places distinguished as permanent, temporary and potential; showing also inhabited areas, villages, factories, barracks, railway, town, etc. Examine the occupiers for parasites, and the houses for anopheline-carriers, which shows the relation to the breeding-grounds. Each place has its own peculiarities. Do not assume, for instance, that the breeding-place of *A. fuliginosus* will be similar in Lahore Cantonment, Dehra Dun and Delhi. The habitat must be actually determined for every species of Anopheles in every locality. Occasionally Anopheles change their habitat in a place because for some reason it has become unsuitable.

Infected anophelines present.—In carrying out an inquiry as to the prevalence of malarial infection in anophelines, it is necessary to catch a considerable number of adult anophelines from the village or quarter in, and adjacent to, which the spleen index and endemic index were determined. If the species acting as vectors have not already been worked out fully,

[1] From section on "Survey of Breeding-Places" by Lt.-Col. S. R. Christophers, C.I.E., F.R.S., I.M.S., in Lt.-Col. G. T. Birdwood's *Clinical Methods for Students in Tropical Medicine*, 3rd Ed.

dissect as many female anophelines as possible, noting the species dissected, those in which oocysts and sporozoites are found, and the sporozoite rate in each. It is necessary also to ascertain which species are not acting as carriers, specimens of each being kept alive for several days and then dissected. Specially note whether the local malarial incidence coincides with the distribution of any particular anopheline; this will not infrequently be found to be the case.

Species vary in the readiness with which they become malaria-carriers, and, for reasons not yet determined, the same species differs in this respect in different circumstances. As a rule anophelines bred from larvæ are not as readily infected as adults caught in nature, but, in the case of adults caught, it is possible that they may have been previously infected. The conditions known to influence infectivity are the atmospheric temperature, age of the anopheline, whether it has been impregnated or not, food already consumed, and other undetermined factors. These latter require thorough investigation, and this can only be carried out in malarial areas.

The habits of the different species of Anopheles carrying malaria should be studied in detail if the scheme of reduction is to attain any considerable degree of success. Any new species of Anopheles met with calls for special investigation. If the observer is not an expert entomologist he should pack a male and female, *secundum artem*, and despatch them to the Director, Central Malaria Bureau, Kasauli, or the Government Entomologist of the province in which he is working (see pp. 62–65).

It is probable that even in a malarious locality only about 25 per cent. of the anophelines are likely to succeed in biting human beings; only one-third of this 25 per cent. is likely to survive for a week or more, and only one-fourth of the remainder is likely to succeed in biting a second person. Hence only 1 in 48 is ever likely to give infection (Ross). This may be true of the whole anopheline population of a district, town or cantonment, but certainly does not hold good for the individual house, hut or tent. The writer has more than once found that every mosquito taken in a tent or hut had fed. Wenyon and Newstead record the same observation. Those mosquitoes that have fed are more important in relation to malaria than those in outhouses. This fact affects the estimation very materially. No method yet devised can give us even approximately the average number of anophelines in a place.

Roughly in India not many more than two or three anophelines are caught in each inhabited room. The writer has at times spent futile hours in searching vainly for anophelines where there were many malarial cases. Often those found have fed on blood and are loaded with eggs. Most get away in the morning. When huts or houses are close to marshes, tanks or breeding-pools there may be a few hundreds to each inhabitant. In highly malarious places a large percentage of the adult anophelines captured near breeding-places are infected. The circumstances in which such captures are effected are very exceptional, and cannot be relied on for routine work as sources of infected anophelines.

It is well to systematise each day's work, *e.g.* using the mornings in capturing winged anophelines, the afternoons in identifying and dissecting them to ascertain if they have oocysts in the stomach wall or sporozoites in the salivary glands. This is the most laborious part of a malarial inquiry and the part that occupies the most time.

Sporozoite rate (p. 139).—The sporozoite rate of an anopheline species means the percentage of females found to have sporozoites in their salivary glands in the *natural* state. It is convenient to include in this anophelines with

zygotes[1] in the mid-gut; when this is done the fact of their inclusion and the number so included should be stated. The sporozoite rate is obtained by dissecting anophelines (pp. 76–78) caught in the area under investigation. In an intensely malarious locality this may be as high as 13 per cent.; in the ordinary endemic malarious season it will usually be less than 4 per cent., and may be even less than 1 per cent In some cases the sporozoite rate is exceedingly low, although anophelines are numerous and the endemic index moderate. It is necessary to state the species of anopheline and the actual house, hut or place in which infected anophelines were taken, these facts being marked on the test tube or bottle at the time of capture. In compiling sporozoite rates it is important to see that the Anopheles are always taken in similar conditions —for instance, not at one time in a hut, at another in a stable or outhouse— otherwise big errors will be introduced and much time wasted. About 100 Anopheles may be dissected and examined microscopically in a day.

Meteorological conditions—rainfall.—(See pp. 21, 22.) Its distribution during the year; torrential or not. Its effect on the population. (Years of deficient rainfall are usually years of scarcity and hardship, years of abundant rainfall are usually years of sickness and high mortality.)

Wind.—(See p. 22 and Fig. 46, p. 134.) Knowledge of the prevailing wind and direction of drift saves time and labour in hunting for larvæ in collections of water, as often we can then almost instinctively go straight to the spot where the larvæ have accumulated.

Temperature.—See pp. 19, 20.

Humidity.—See pp. 20, 21.

Economic, social, domestic and hygienic conditions.—In an endemic malarious area these conditions give a good idea of the effects of malaria, and the degree of relative immunity acquired. They must be specially alluded to in the Report. This information is easily acquired . price of food and clothes, degree of unemployment and poverty. or abundance of work and prosperity, state of sanitation and so forth; it may therefore form one of the last parts of the inquiry.

Communications.—Roadways, railways, tramways; river boats, steamers, ferries, quays, river crossings, and extent of intercourse with different areas. This has special reference to possible imported infection and the carrying of infection to the neighbouring localities or farther afield.

Having made a series of observations regarding malarial fevers located in special malarial centres, the particular breeding-pools of malaria-carrying anophelines, and ascertained the huts or houses they favour, it might be thought that we should be in a position to explain scientifically and satisfactorily why malaria prevails in some places and not in others. We are obliged to confess that this is by no means always the case. There is still much about the habits of mosquitoes and regarding the endemiology and epidemiology of malaria we do not understand.

Whilst the subject of anophelines is of vast importance in the study of malaria, it will be seen that there are other important factors which determine the prevalence of malaria in a locality, and it is necessary that we should be able to give the exact relative values of these factors in an investigation. Unfortunately our limited knowledge of these factors at present does not permit of the estimation of these relative values.

Possible errors to be eliminated.—All calculations as regards the actual malarial intensity of a particular locality, to be reliable, require the utmost care,

[1] We should remember, however, that in some species of Anopheles the malaria parasite does not develop beyond the zygote stage (Table, p. 102).

and the elimination of *possible errors*. The same remark applies to each of the factors regarding which information is collected. Such inquiries always mean hard work. Anyone who has taken the endemic index of malaria in even a comparatively small district containing, say, 1,000 children, for a period of six consecutive months, tabulated in age-groups by the month for different villages, knows the amount of labour involved; and that, usually, in somewhat trying circumstances, apart from the possible opposition of the people themselves.

In estimating the value of statistical inquiries in malarial diseases, as in other infective maladies, one should invariably keep in view the degree of *probable error* in each calculation. In this connexion POISSON's *formula* may be of some use in dealing with small groups of data. The formula itself, of course, only deals with the actual figures applied to it. It has nothing to do with the various sources of error liable to be met with in the figures themselves, such as errors in observations, defects in the actual units employed in the group of figures, etc. The wide degree of variation in future identical groups as shown by POISSON's formula indicates how essential it is to have a reliable number of observations to work on before arriving at positive opinions. With faulty observation the multiplication of figures can only magnify the error and lead further astray.

Recording the results.—When recording the results of the survey take care to give adequate consideration to the following: Nature and extent of supply of Anopheles; prevalence and distribution of adult Anopheles; prevalence and distribution of human malarial infection; mortality and sickness; any economic conditions affecting malaria in the area under survey; projection of the main endemiological and epidemiological facts concerned in their complete aspect.

In regard to the nature and extent of supply of Anopheles, consideration should be given to—local supply from breeding-places in the area; infiltration from neighbouring area and importation. Give also proportionate importance to breeding-places of the following kinds—breeding-places of the *first order*, actually among the houses or very close at hand, say within 100 yards; breeding-places of the *second order*, at a greater distance, up to 400 yards (distance of habitual flight); breeding-places of the *third order*, larger sources at a greater distance than 400 yards. Consider also—the actual breeding-places seen; and potential breeding-places.

Unlooked-for difficulties are almost certain to arise in carrying out any anti-mosquito scheme; this is particularly so when the survey is connected with a number of incomplete and uncertain factors. In such cases due latitude must be allowed for any modification of the scheme that may subsequently prove to be necessary.

RURAL MALARIA SURVEY

The bases upon which a rural survey is conducted are the same, *mutatis mutandis*, as for a town or a military cantonment. In connexion with the following remarks the reader is asked to run over what has been stated in PREVENTION OF MALARIA IN VILLAGES IN INDIA.

It is necessary to acquire some familiarity with the area to be surveyed by consulting the Imperial and District Gazetteers, Reports of Director of Public Health of the Province, Assistant Director of Public Health of the District, Assistant Director of Public Health (Malaria), Census Reports, previous local malarial inquiries (if any), works on the general history and natural history of the district, and by the study of good maps.

In the practical work note the areas most densely populated and the localities that are considered to be the most malarious. From the vital statistics ascertain any facts recorded regarding the occurrence of epidemic malaria. Decide after a preliminary cursory reconnaissance what features demand research and select suitable test areas for the early work. Make a malaria survey of as many villages as possible. Describe the general and special features of the surrounding country, character of the soil, depth of the subsoil water, and note whether there is any liability to flooding. Observe the race, main occupation of the people, their relative prosperity or the reverse. Ascertain the distribution of malarial infection throughout the area, the species of Anopheles occurring in the area, the nature of the breeding-places of each and their relation to human infection, the chief insect carrier or carriers in the area: note any state of affairs which seems to be responsible for a high degree of malaria in any or all of the villages, and the most important steps in the reduction or amelioration of the effects of malaria in the area.[1]

Investigation of European malaria.—As in the cases of town and village inquiries, a map should be made of the houses or barracks occupied by the persons under investigation, the breeding-places of anophelines within half a mile marked down, and the positions of all native quarters noted, the map, of course, being drawn to scale and the distances entered.

The blood of as large a number of Europeans as possible in the locality should be examined and the temperatures taken, ascertaining also by specific inquiry in each case whether quinine is in use. Note the number having parasites or gametocytes; where no parasites are found the presence or absence of a relative increase of large mononuclears or of pigmented leucocytes should be noted. These points can all be ascertained from the one stained slide of each case. Note whether any section of the Europeans, or those occupying particular quarters, have a larger percentage of malarial infection. Record the conditions in which they are living—near native quarters or breeding-grounds of anophelines, state of houses as regards protection by wire-gauze doors and windows, use of mosquito nets, electric fans or punkahs, etc. Specially note those groups of Europeans taking quinine regularly or otherwise, and any relation between the European malaria and nearness to native huts.

Inquire specially into the state of malaria in neighbouring huts by blood examination, the percentage of infected children in each group of huts, degree of malarial infection in adults, number of anophelines present—roughly speaking, abundant, scarce, or cannot be found, and in the last-named case test pools should be made.

Ascertain the species of anophelines present and their relative numbers; the sporozoite rate for each species; map all breeding-places, noting what kinds of larvæ are found in each. "Capture as many anophelines as possible in European houses or barracks, especially in the early morning; look in mosquito nets; determine their species, sporozoite rate, and whence derived."[2]

Investigations into the malaria of a locality, to be accurate and reliable, should be continued in the place throughout the entire year, beginning, say, in August or September. During the year make a record of *seasonal variations* in the endemic index (children under 10 years); seasonal alterations in number of anophelines present at all times during the year; distance of flight of anophelines from their breeding-grounds; sporozoite rate in anophelines at different periods of the year.

[1] Lt.-Col. S. R. CHRISTOPHERS, C.I.E., O.B.E., F.R.S., I.M.S., in Lt.-Col. G. T. BIRDWOOD's *Clinical Methods for Students in Tropical Medicine*, 3rd Ed.

[2] STEPHENS and CHRISTOPHERS, *Practical Study of Malaria*, 3rd Ed., p. 215.

There are places where malaria-carrying anophelines exist in large numbers without severe malaria, side by side with other places where both severe malaria and anophelines exist. This has been definitely shown in the work carried out by experts in India, and without entering into the details of the special instances in which it has been met with, it is here stated as a fact which still remains unexplained.

Report on the Malaria Survey

The data collected and the observations made should be fully considered and classified with a view to preparing a clear and concise report on the local malaria and how it is to be reduced. It is essential to have a precise and definite opinion as to the local conditions responsible for the existence of the malaria, and a knowledge of the factors which, if abolished, would greatly reduce it, or perhaps get rid of it altogether. Often, after a malaria survey, with complete and accurate data in hand, the solution of the local malaria problem is the easiest part of the task. The writer recalls an instance in a large military cantonment in which, after a malaria survey, a deep (9 feet) drain a mile or so in length, lined at the bottom to a height of 3½ feet, with "weep holes" every 30 feet, was dug; it dried up nine large breeding-pools, lowered the level of the subsoil water and materially reduced the malaria in two regiments in nine months, and the cantonment has had a comparatively low malarial incidence ever since.

The extent and scope of the report itself depend on the purpose to be served. Assuming that it is for the adoption of practical anti-malarial (including anti-mosquito) measures, it is advisable to arrange it in four parts, consisting of—an introduction, summary of investigation, opinion arrived at and recommendations. The introduction would give the terms of reference or recite the circumstances calling for the survey, its object and scope, historical, physical and social features of the town, cantonment or district and particulars regarding its inhabitants. The summary of the investigation should be fairly complete and embrace a statement of each of the items leading to the exact measurement of the amount of the local malaria, and the part that local malaria-carrying Anopheles are playing in the area. In addition this part of the report should give the amount, distribution and nature of the malaria, the way it has arisen and how it is being maintained, disseminated, intensified or otherwise changed in the area under report. Also a comparison of the locality with one having an average malarial incidence as regards—endemic index, spleen rate, sporozoite rate, Anopheles, especially malaria-carrying species; future possibilities for importation of infection, immigration of non-immunes (if many, this is of importance in ordinary endemic areas as leading to intensification of malaria in the permanent inhabitants; see pp. 48, 49). It should likewise include tables of statistics of current malaria, spot maps, sketches, photographs of breeding-places, plans showing relation of the latter to the areas of special prevalence, and such other illustrations as the director of the survey considers essential. This is a most valuable part of the record, showing the exact state of the malaria of the locality at the time of the malaria survey, and its causes. It will be a priceless possession for all time.

From a due consideration of the summary an opinion is recorded and a definite, practicable method of dealing with the local malaria stated, bearing in mind the financial and other circumstances of the place. In most instances financial considerations are of fundamental importance. An elaborate

report, embracing possibly every endemiological and epidemiological fact connected with the malaria of a locality and a detailed description of how eradication or mitigation would be effected, is of little use if the cost of the measures advised is altogether beyond the amount of money available or obtainable for the work. The recommendations of the report should be as short as possible—sound, clear, concise and complete. It is the part of the report first read and the one acted upon.

The recommendations should show—the necessity or relative urgency of measures for the prevention or reduction of the malaria in the locality under reference; the conditions involved as regards anti-Anopheles measures; exact scope, nature and extent of drainage works advised, the position regarding introduction of a public water supply to replace wells which are breeding malaria-carrying Anopheles; screening of houses, and any other local operations; arrangements suggested as regards quinine treatment of local malaria if this is considered necessary; and any economic conditions that call for attention.

All reports dealing with major operations, such as drainage, measures for lowering the level of the subsoil water, diversion of streams, screening of barracks, houses, etc., should give details of this work and its cost, prepared by an engineer.

If the town, cantonment or district is extensive and malaria widespread, it will usually be sound to advise the appointment of a special malaria officer to carry out the measures recommended in the Report, arrange the programme of anti-malarial work for the malaria staff, supervise all preventive measures, including treatment to prevent relapses, keep malaria records up to date, watch seasonal changes in the malaria, and variations in Anopheles, especially the known malaria vectors.

At the beginning of any lengthy report give a *Table of Contents*, and commence the report itself with a very *brief synopsis of its construction*; at the end give a full *Index*. The report should, if feasible, be printed or typed, and several spare copies retained. A report is sometimes lost or mislaid, and it is an extremely difficult undertaking to rewrite one, say, a few years later, as the author has been ordered to do more than once. Had he not retained his diaries, the task would have been impossible or very indifferently carried out.

II.—Education of the Public in Anti-Malarial Measures

Given an intelligent community, possessing a knowledge of the manner in which malaria is communicated, and the ability and willingness to apply that knowledge, there is no reason why malaria should be the serious menace to public health that it is. Perhaps the greatest task, then, is an educational one —to convince the masses of the importance of health, and how to prevent malaria. This is a huge undertaking with a population having fatalistic beliefs, steeped in superstition and prejudices. If we succeed in the educational part of the work, all is well.

If the history of malaria among the civilised be studied, it will be found that there is not a single instance in which eradication of the disease has been effected by action or initiative taken by the uneducated classes; it has always been due to State organisation and effort, or to the enterprise of commercial companies, often aided by the wealth of rich philanthropists. Health lessons should be given in all schools, supplemented by suitable diagrams and models. It is unnecessary to go deeply into the subject of malaria. The children should

be told the part played by mosquitoes generally as disease-carriers, without referring to genera or species, wing markings, etc. Teach the children how to recognise a mosquito in the larval, nymphal and adult stage, and leave it at that. Tell them what they can do to prevent mosquitoes breeding in and near their houses, how the infection is probably acquired in the houses, and how they can catch and destroy the adult insects there. Emphasis should be laid on what cinchona febrifuge and quinine can do. Outdoor demonstrations are invaluable. An hour spent in carefully explaining the part played by mosquitoes in regard to malaria will often arouse a group of young villagers to search for and render harmless breeding-places and destroy adult mosquitoes.

The writer would like to emphasise the educative value of a few anti-malarial campaigns in endemically malarial towns and military cantonments. They could be easily organised and carried out. During their progress public attention should be riveted on the work. These demonstrations should concentrate on a few places in each province, and all reasonable means needed for them should be provided.

The following remarks of LE PRINCE deserve the serious deliberation of statesmen in India who deal with public health work: "Considering the fact that a few years ago hundreds of communities were seriously affected [with malaria], and with no apparent relief in sight, that the public in general had no visible proof of the possibilities of malaria eradication, and too large a proportion of our public was wrongly informed regarding the cause of malaria, it is gratifying to note that this year over 100 of these same places have decided to finance campaigns for malaria elimination. They have already appropriated for this season's work nearly twenty times as much as the original annual Federal appropriation, 1914–1917. It is even more encouraging to note that there is a strong demand for state and county aid along these lines, and that such support has already been given, and has the approval of the public. What is also important is that a large part of the public now realise that it costs them much more to continue to suffer and support the financial loss caused by malaria, than it does to eliminate the disease from their community." The last remark embraces a serious truth. The average town in India can free itself from malaria for a quarter to a third of the sum which it costs to endure it. "It has been definitely demonstrated that many of the localities so affected can eliminate malaria at a reasonable cost, and that the best way of inducing the public to do so is to carry on carefully planned demonstration campaigns in badly infected areas. The result of such campaigns means a much larger annual income for the community, the county, the state, and the Federal Government. Preventive malaria work is in reality a sound business investment. Up to 1913, no county or state made any appropriation for malaria-control operations, although the value of such work was proved twelve years previously." [1]

The growth of knowledge regarding the nature of malaria and its prevention among the people of India is necessarily slow, especially in rural districts, but even in these something useful is being done by means of itinerant dispensaries, demonstration camps and instructors, and the cheap sale of quinine and cinchona febrifuge. In towns, however, with their municipal hospitals and medical and sanitary staff, there is no reason why the people should not be made familiar with their greatest enemy and the defences to be used against him. In anti-malarial sanitation we want the intelligent help of everyone possible. This essential education of the public may be carried out somewhat as follows. Let the people know what LAVERAN, MANSON, RONALD ROSS and

[1] LE PRINCE, *Annual Report*, U.S. Public Health Service, 1920.

others have discovered, and that malaria is the worst and most costly disease in India. There should persistently be used as anti-malarial propaganda, lantern lectures, demonstrations of adult mosquitoes, and of anopheline larvæ in the town tanks or the village pond or other known breeding-places; exhibition of patients with enlarged spleens, chronic malaria and malarial cachexia; issue of illustrated leaflets on malaria, picture postcards showing the effects of the disease and so forth. The people all over India should know the cost of malaria to the State, to employers of industrial labour, planters and merchants, and especially to the working-classes themselves.

Medical men, sanitary officials, civil servants, and schoolmasters throughout India should make every effort to diffuse knowledge of malaria amongst the less informed classes of the population. In towns, civil stations and military cantonments *periodical* lectures on malaria and its prevention, and the part played by anophelines in the dissemination of malaria, are useful, serve to maintain interest in the subject and enlist co-operation of the people.

In the light of our recent knowledge architects and engineers in India should studiously consider the various new problems in anti-malarial sanitation. It is not intended that these views should upset all the building traditions in the malarious parts of India; these cannot be ignored; what is required is the adaptation of new dwellings to the requirements of present-day sanitary principles.

All engineering students in India should be taught the evil effects of creating borrow-pits unnecessarily, the risk of unbridged embankments and other public works that raise the level of the subsoil water; and the principles of anti-malarial measures now employed by all civilised Governments and peoples should form part of their curriculum of studies.

The town hospitals and dispensaries should be centres, not only for the treatment of malaria cases, but also for educating the masses as to the nature of malaria and how it may be prevented. The establishment of malaria clinics is referred to at p. 372.

We should not, however, be too optimistic in hoping that education of the masses will bring about great immediate reduction of endemic malaria. It is now fourteen years since the late Dr. J. A. Turner, Health Officer of Bombay, sent the writer copies of the leaflets, placards and pamphlets on malaria distributed throughout that city with exceptional liberality. Lectures with lantern-slide demonstrations were also given in various parts of the municipality; yet Bombay has still its periodical outbreaks of severe malaria. For the last sixteen years it has been known that *Anopheles stephensi*, the sole malaria-carrying mosquito in Bombay, breeds in private wells; but the Hindu in the city has religious prejudices against fitting any form of pump to wells, and against a public water supply; he uses the well in his compound. The closure of these private wells and the universal use of a constant public water supply on modern lines, which would remove the necessity for all storage of water on premises, would almost certainly eradicate malaria, or at least very greatly decrease its prevalence. The same holds good regarding certain parts of the cities of Madras and Calcutta. Nevertheless, educating the masses is one of the great anti-malarial measures in India. It will, among other things, aim at an improvement in their economic condition, which is a fundamental necessity in malaria reduction. In this education, pictorial methods are perhaps the most effective. Illustrations of the mosquito should be placarded universally; every quinine and cinchona febrifuge packet should have a picture of a mosquito on it, and "The Enemy," "The Beast," or some such designation applied to it. Every official paper,

newspaper, notice, etc., should give a representation of that wily and elusive insect. The writer would go so far as to have the coinage stamped with it.

The engineer in India deals with large undertakings—road, railway, bridge and building construction. The sanitary engineer is called upon to drain malarial swamps, lay subsoil-water drains, erect dams to prevent flooding of rivers, etc. It would facilitate his work were he acquainted with the main object in view—the reduction of mosquitoes. Hence an elementary knowledge of entomology, including the bionomics of mosquitoes, is very useful to him. In this the malariologist can help the engineer, just as the engineer can help the malariologist. The co-operation of these two is indispensable if the best anti-mosquito results are to be attained. The writer would here like to put on record his great indebtedness to many engineers in India for the help they have given him in anti-malarial work. Once the engineer understands the problems to be settled, he, as a rule, will carry out what is required in an efficient way. Medical men should co-operate with engineers in devising definite anti-malarial plans, and convince them that all engineer-made anopheline breeding-places and all building-malaria are deadly professional sins. The following advice is given to inexperienced sanitary engineers who are engaged in anti-malarial work, and desire to be of real assistance to malaria and sanitary officers in India.

Axioms for young sanitary and municipal engineers engaged in malaria work in India.—1. In areas where malaria prevails do not fail to consider standing or sluggish water as a menace to health during the breeding season of Anopheles, and its removal or control probably of much importance.

2. Consider undrained borrow-pits as a potential danger that should not be allowed.

3. Wherever possible, culverts must be so placed as to drain the bottom of all wet lands in the culverts' drainage area, and not to interfere with future small drainage projects on farm lands, rice-fields, etc. (Fig. 99).

4. Do not attempt to drain seepage outcrops with crowfoot ditches when intercepting ditches are necessary (Figs. 100–102). In making intercepting ditches the excavated material should be placed on the down-hill side of the ditch.

5. Do not allow contractors or others to dig wide-bottom ditches along highways and roadways where narrow-bottom ditches can be used, and see that those ditches are dug to proper grade, so as to retain a minimum of stagnant water (Fig. 89).

6. Do not fail to use your influence for the proper maintenance of roadway and railroad ditches, particularly near residential areas.

7. Municipal engineers should advise town council commissioners to have all roadside pools eliminated, to prevent water standing in roadside ditches in town suburbs, and make every effort to have this necessary work accomplished.[1]

Publicity propaganda in anti-malarial campaigns.—One of the most potent accessories in an anti-malarial campaign is publicity propaganda skilfully handled. It should be remembered that the entire work, viewed in its broader aspects, is largely an educational effort, and if this be a sound statement, then the tuitional end is at least of as much importance as the reduction of Anopheles. By it the people are being taught to defend themselves, and this incorporation of personal endeavour reduces the work all round, and the expenses. This publicity should go on without interruption, and not cease as soon as any one measure is taken in hand. Keep up a constant flow of publicity from the time

[1] *Malaria and the Engineer.* A Treatise for Technical Students. National Malaria Committee, U.S.A., 1922.

the work is first broached, to and beyond the end of the campaign. For instance, as soon as it is definitely decided that a campaign is to be started in a town, the director of the work should explain at a public meeting the scientific facts upon which the work is based, refer to the great successes of similar work in the Panama Canal Zone, Federated Malay States, Algeria, Italy, Cuba, Ismailia and elsewhere, and then speak about the local malaria problems, and the methods to be employed in dealing with them. As the work progresses, he should issue statements as to the advance being made, *e.g.* the amount of drainage finished, organisation and work of the oiling gangs, the work of the inspectors and overseers; if fish control is started, the basis on which it operates in reducing malaria, establishment of aquaria, method of stocking streams, ponds, cisterns, etc., with larvivorous fish and so forth. The works in progress should be referred to in the newspapers circulating in the neighbourhood, vernacular and English, from time to time, soliciting the co-operation of all members of the community in carrying out the campaign.

Training in malaria work for medical men and women.—Education in tropical medicine in India is now on a very different basis from that obtaining forty years ago. The writer is most hopeful that the School of Tropical Medicine in Calcutta, which is in the hands of experts of wide reputation, will give a great impulse to the advancement of our knowledge of malaria. The greatest progress will be made by the physician, pathologist, tropical sanitarian, protozoologist, biochemist and pharmacologist working together and dealing with all aspects of the malaria problem. There is no country in the world that offers such extraordinary facilities for solving the unknown and doubtful problems connected with malaria as does India. The acquisition of such knowledge, however, is no easy task, and the writer believes it will require all the expert skill available for another generation or more before all that is essential for the combating of malaria is discovered.

Before the Great War malaria classes were held under the auspices of the Central Malaria Bureau, Kasauli, to train medical officers, assistant surgeons and sub-assistant surgeons in anti-malarial work and malaria research. *Without such knowledge everything is aimless.* The writer knows from several years' experience of the work of officers so trained that these classes were of the highest value to India. They have only just been re-started. It is of supreme importance that they should be maintained. It would be a great calamity, and a wanton waste of available material, were anything to interfere with their continuation.

The direction of anti-malarial measures in the Indian Empire is in the hands of the Medical Research Workers, a highly expert body of scientists, who take a sound and comprehensive view of the malaria problems of India. The writer pleads that this organisation of ardent workers be given Government and public support.

In most provinces now there is a trained malariologist, who holds the position of Assistant Director of Public Health, and guides the malaria work of the province. There should be one such officer in every province. These men are doing indispensable work of the highest order, and should receive all possible administrative and public support. Their life is not cast in over-pleasant places. All malaria research work, however, should be co-ordinated by the Central Research Committee and by a special Director under the Government of India.

At the All-India Conference of Research Workers held in Calcutta October 27 to 29, 1924, the sub-committee appointed to consider the order of priority of research to be given to the different groups of diseases requiring further scientific investigation *placed the malaria group at the head of the list,*

and this was accepted. The Conference recommended that the following staff should be employed on a semi-permanent basis for malaria research work: a director, assistant director, entomologist, one assistant surgeon, two sub-assistant surgeons, draughtsman and photographer, laboratory attendants and *chaprassis*. It was agreed that an experimental station in connexion with this inquiry should be organised, the most suitable place for continuous work being selected from time to time. The work is to include—the study of such problems as the cause of malarial prevalence, distribution and intensity of malaria in India, the nature of epidemic malaria, effects of malaria, *e.g.* on the rural population, the causes of hyperendemicity, and the reasons for the existence of malaria-free areas where infection would normally be expected. The research staff are to work continuously on—the parasites of malaria, anopheline vectors (including transmission experiments), bionomics of anophelines, circumstances affecting breeding, food of larvæ, study of larvicides, larvivorous fish and natural enemies of larvæ; treatment of swamps, rice-fields, streams and sub-soil drainage; experimental anti-mosquito measures, and the subject of screening of habitations. They will also study the subject of continuous infection, relapses and quinine treatment; advise Government on anti-malarial measures; and report on the necessity for anti-malarial operations in particular regions, and the form these should take. The results of the work should be published. Lastly, the very important matter of training medical officers and assistants in malaria work will be taken in hand. It may confidently be predicted that work of inestimable value to India and to all malarious countries will result from this solid effort to solve the more important of the unsolved problems that at present hinder progress. The greater the amount of research, the more will the cost of anti-malarial measures be reduced.

The more work done on malaria in the field, in the laboratory, and in the hospital—the study of malaria-carrying anophelines, of the life-history and structure of the parasite, of the action of quinine in malaria—the more complex the subject of malaria seems to be. In the course of his official duties in India the writer carried out scores of malaria surveys, and he believes that in every one of these of any dimensions he learnt some new fact connected with malaria. This is the experience of all practical workers who have had to devise measures for reducing the disease.

III.—Expenditure on, and Limitations of, Anti-Malarial Measures

Limitations to expenditure.—There are limitations to expenditure in connexion with anti-malarial work regarding which we should have definite opinions. Theoretically the limit of expenditure in this connexion is the amount that malarial diseases cost the country. Malaria is expensive by reason of the deaths it gives rise to (which imply a corresponding loss of production), the actual cost of illness, the loss of labour from malarial fevers in many millions of people (which loss is more obvious in localised collections of labourers working on railway embankments and irrigation canals, and in various industries such as tea gardens, factories, etc.), sickness and inefficiency amongst Government employees, including sickness, deaths and invaliding amongst officers and troops, etc.

The limit of what may profitably be spent in anti-malarial work, provided it is effective, is determined by such considerations. Were it possible to estimate the sickness due to malaria in the Provinces in proportion to that due to all other causes, we should be in a position to state how much might legitimately be expended on malaria. At present we are unable to gauge this even roughly. In the cases of the Army in India, and of jails and asylums, we can with more or

less accuracy state that malaria is responsible for about one-fifth of the sickness rate, and this places a limit on the amount of the budget allotment that should be expended on anti-malarial measures. The writer knows of no records which show that expenditure on the prevention of malaria has been systematically estimated for. The expenditure on malaria by the Government of India and the Provincial Governments is, in fact, limited by the amounts allotted in the medical and sanitary budgets, and in periods of epidemics by the special grants.

A special malaria tax in areas of endemic malaria.—It is with regret that the writer finds himself compelled to express the opinion that the time has come to consider the advisability of introducing a regular malaria tax in all endemic malarious districts throughout India. There are, apart from financial necessity, several obvious reasons for this innovation, among them the facts that it will keep the question of prevention of malaria alive, and at a low cost maintain a universal propaganda to effect its reduction. The tax should be very small and compatible with the means of the people—the revenue collected on this account should be expended exclusively on anti-malarial and anti-mosquito measures.

Economical campaigns against malaria should be directed against those species of Anopheles that are known to be the local carriers of malaria parasites, which must in each case be determined and not assumed. If the local carrier or carriers and their favoured breeding-places are not determined, anti-malarial measures indiscriminately carried out may lead eventually to a worse condition than previously existed by making the breeding-places of harmless mosquitoes into favourable places for malaria vectors, and the money spent will be more than wasted. If further economy were compulsory the campaign might be confined to the period during which Anopheles are infective. This period is ascertained by systematic determination of the sporozoite rate, and by a consideration of the factors necessary for the development of malaria parasites in Anopheles. "From what I have seen of the results of radical measures, I feel strongly that by radical measures will the end be attained soonest; that every success will help others; that people will be saved who will never consent to take quinine in sufficient doses, if at all; and that only by radical measures will be stopped the infection from, and the death of, the vast mass of those who suffer from malaria *sine* pyrexia, those who fail to recognise they suffer from malaria, who account for a very large percentage of the death-rate of a malarious community." [1]

As Sir MALCOLM WATSON elsewhere adds: "On the outskirts of his handiwork there lurks the ever-vigilant anopheline ready to take advantage of any slackness or relaxation on man's part. A cleared jungle, if left without cultivation or attention, is in a few years again a malarial focus. But a few miles away is a jungle that was never malarious, yet without investigation it was cut down and burnt and became a focus of endemic malaria. We are learning the meaning of some of these enigmas; we must know the solution of them all before we are able to control malaria properly. We have seen why malaria appears, varies in severity and then vanishes, although initially there is little to explain matters. With the knowledge already acquired we are now in many cases able to advise with confidence how malaria in particular areas may be controlled. It is all but morally certain that the day will come when we shall be able to control, if not eradicate, malaria everywhere with facility, and will do so at a cost that to us at present seems incredibly low."

[1] Sir MALCOLM WATSON, *Prevention of Malaria in the Federated Malay States*, 2nd Ed., p. 128.

"We have hardly begun the great campaign against malaria yet. In the past twenty-five years we have been scouting rather than fighting. Different places require different methods of attack. A method successful in one place may aggravate the disease in another. We do not know why one species of Anopheles is a carrier of malaria, and another, hardly to be distinguished from it, is not. We do not know why one species lives in one breeding-place and another species in another. We do not know why one rice-field contains one group of Anopheles, and another contains another group."[1] The writer takes the liberty of endorsing these very comprehensive remarks.

In India, in former years, many houses, villages, or even whole towns, were built on sites that are radically unhealthy, and the cost of converting the houses, villages, or towns into healthy places would be unjustifiable.[2] Reference is made to one such town on p. 366. It may be that the site is on the banks of a river that periodically overflows, or on the edge of a dying river with numerous ponds and pools, or that it is in the immediate neighbourhood of an undrained, extensive marsh or swamp. In these cases it is sometimes cheaper to relinquish the house, village or town and erect another on a selected healthy site, rather than to undertake measures to control the mosquitoes in the old site.

Quinine versus anti-mosquito measures.—Whilst the cinchona alkaloids have a most important place in the problem of reducing malaria in India, those dealing with anti-malarial administration should remember the limitations of the usefulness of these remedies and preventives. Quinine cannot be considered a satisfactory substitute for anti-mosquito measures. Quinine, when properly used, will cure malarial fevers, but it will not prevent further infections. Quinine administration carried over a period of years may be more costly than anti-mosquito measures; the former is temporary in its effects, the latter may be permanent. We must constantly bear in mind that quinine (or other derivative of the cinchona plant) is used only by about one-seventh of the people who suffer from malaria; the other six-sevenths are working out an immunity. Millions die in the attempt to acquire immunity, chiefly children, while those who do acquire it go through years of suffering, and for the time being are wrecks of childhood and manhood. It is the work of the statesman, anti-malarial sanitarian, and especially of the educated and better-class Indian and landowner, to eliminate the suffering experienced in the immunising process, and to help the people to acquire immunity through healthy environment, better houses, and better food.

Of other measures, mosquito nets and the screening of houses from mosquitoes help to prevent infection, but they can only be of use to a comparatively small proportion of the population, partly on account of their expense and partly because their use requires a state of education not yet reached by the masses. To make a serious impression on the malaria of India, the Anopheles which carry it must be reduced, or something in the form of a cheap super-quinine must be discovered and made available in unlimited quantities.

The malaria problem must be faced in all its grimness; it is far the greatest problem that confronts the administrators and people of India. All sanitary opinion indicates that it is largely a financial question. It has been suggested that loans for anti-malarial measures should be launched, and it is considered that the improvement in the health of the people and in the land agriculturally

[1] Sir MALCOLM WATSON, opening address, Fifth Biennial Congress of Far Eastern Association of Tropical Medicine, Singapore, 1923.

[2] Up to the present day business companies dump their factories wherever they think fit and call in a medical man or malaria expert when they find their labour force impregnated with malaria and unfit for work.

would, in course of years, meet the outlay. Sir MALCOLM WATSON says: "It is here I think a Government can help to break the vicious circle which makes the malarious poor and the poor malarious, and can assist a people to initiate drainage works, which from poverty they themselves cannot begin; even if Government cannot pay for drainage works out of revenue, then by pledging its credit a Government can obtain money on loan. Both capital and interest can be paid by assessment of the land benefited." [1]

Even with all the knowledge we have accumulated regarding the natural history of malaria it is not necessarily easy to control. Experience has shown that it is extremely difficult to eradicate, sometimes even to reduce the disease, where it is severe; in some places it seems to be impossible when only the ordinary methods are employed. But, as a rule, the reduction of endemic malaria is a feasible proposition everywhere. The writer's experience, referred to with reluctance, nevertheless merits emphasis. Wherever in military life he carried out anti-malarial campaigns lasting a year or more, the malaria went down considerably. In the Burma Division, after twenty-one months' work, it was decreased by 74 per cent., in the Poona Division, after thirteen months' work, by 51 per cent., and so on in other divisions in which he was administrative medical officer. These facts may be found in the official records. It is scarcely necessary to say that this was not achieved by sitting in the office chair.

Up to the present, malaria in India has only been toyed with, and that perfunctorily. A few drains have been dug here and there, kerosene oil has been largely used in a wasteful and indiscriminate way on surface waters, itinerant dispensaries have been sent to the districts for a few months at a time, and quinine or cinchona febrifuge has been distributed free in some places. Such measures cannot and will not solve the malaria problem in India. Those hard-worked malaria officers in India, who take the broad view, know, perhaps better than the writer, the truth of these statements.

What is wanted is an intensive anti-malarial campaign throughout India for a whole generation, the work of which is participated in by every village in the country. It is supererogatory to state that this cannot be undertaken by the Central Government or Provincial Governments, by the Central Research Committee or by Provincial malaria officers. No Government in the world could face such a task with any hope of success. It must be undertaken by the people themselves, especially by the educated and wealthy classes. If during this long campaign India would divert some of her attention from politics and think of her health she would raise one of the richest and finest races in the world. The Central and Provincial Governments and their technical staffs can formulate schemes for the commencement of this campaign, and help and guide it through the long years it must be continued. The present Co-operative Societies, expanded and working universally, would absorb the lion's share of the anti-malarial work. With such a scheme there would be an enormous increase in the demands for cinchona febrifuge and quinine, and as it takes at least eight years for the cinchona plant to produce the required bark, the sooner many millions of additional cinchona plants are put into the ground the better. It is likewise a *sine qua non* that the manufacture, control and distribution of the products of the bark should be in the hands of the Government, to ensure that their price is regulated and kept down so as to be within reach of the masses. See Appendix I, p. 440.

The writer is convinced that only on these lines will any serious impression be made on malaria in India. It is quite possible that he has overestimated the length of time it will take to achieve the end aimed at. It is well known that

[1] *Prevention of Malaria in the Federated Malay States*, 2nd Ed., p. 128.

once malaria begins to decline, if the anti-malarial work is maintained, the ratio of declension rises rapidly.

IV.—Economic and Sociological Questions connected with Malaria in India

Main causes of ill-health among the masses.—The main general causes of the present unsatisfactory state of health of the indigenous masses of India are—veneration for bovines and other animals that eat or destroy the food required for human existence, economic stress, uneducation and certain religious prejudices.

The rural population is to a large extent illiterate, poor, inert, hard to move, and helpless; they accept with deplorable resignation the blows of fate. The people make little struggle to improve their standard of living, and see little value in such education as is at present available in rural districts. They suffer from preventable disease, pay a heavy toll of life to improper sanitation, give no thought to proper food, and endure illegal exactions without protest. They will not accept responsibility for their backward condition, and respond but feebly to the stimuli which arouse most civilised peoples. The workers under the joint family system support the indolent, a fact which retards progress for all; the agricultural holdings have to be divided into scattered plots, often too small to give an economic return. Early marriage brings children, and too many of them, to young, immature women before they are old enough to look after them; the result is high infant mortality. These are factors handicapping India's economic and social life, perpetually and with tremendous force. Early marriage of youths interferes with their mental and physical development. The mothers, having no education, can impart none to their children. Their seclusion in some sects and their absence of travel make them narrow. Caste is a dead weight which India is always carrying—her heaviest handicap in civilisation.

Veneration for bovine life.—From the presence of 140 millions of bovine cattle in British India there results great competition for the produce of the land. The cost of keeping the useless surplus cattle that are too old, too young or unnecessary for economic life has been estimated to be over Rs. 1,50,00,00,000, or £117,000,000, a year; the land revenue of British India is 30 crores, so that the economic loss due to surplus cattle is over four times the land revenue, and greater than the total revenue. This is a staggering price to pay for veneration for an animal. Besides this there are many millions of ponies, donkeys, camels and goats. If the people would keep their animals down to the number actually required for work and food, there is little to prevent India from being a very prosperous country.[1]

Notwithstanding this vast accumulation of cattle, Indian legislators state that there is a shortage of milk, and that this deficiency accounts for the high infant mortality. The essential cause of any deficiency that may exist is the very small yield of the Indian cow. The average yield of an Indian cow during the whole period of lactation is about 800 pounds. "Contrast this miserable result with the yield of cows produced at the experimental farm at Pusa. Within the last fifteen years the yield of the Montgomery herd on the Pusa farm has been doubled through selective breeding. By cross-breeding, moreover, a type of Ayrshire-Montgomery has been produced which yields 50 per cent. more milk than the Montgomery cow. Some of these cross-breeds, indeed, have given 12,000 pounds in a lactation period, which represents fifteen times the yield of the average Indian cow. The solution of the milk problem will

[1] H. Calvert, "The Wealth and Welfare of the Punjab," in *The Round Table*, July, 1925.

be attained by such cross-breeding and by thus reducing the enormous number of animals which must now be fed and housed."[1]

It is possible, by degrees, to raise the standard of the milch cow; but were one of the animals, capable of yielding 12,000 pounds of milk with each lactation period, fed in the same way in which the present 800-pounds yield indigenous cow is fed, its yield would soon be as small as that of the Indian cow. It is most important that instruction in the feeding of cattle should be imparted to Indian agriculturists, so that the existing animals may increase their production of milk, and when this idea has been engrafted and practised, the heavier animals might be gradually introduced. Breeding of improved types of cattle will not be systematically effected until the agriculturist and cattle-owner know how to feed their cattle and put that knowledge into practice.

The continued *use of animal refuse as domestic fuel* (*bratties, uple* or cow-dung cakes) and as a *leep* for mud floors, instead of its enriching the soil as it does in all other civilised countries, should be easily remedied. Abrogation of this perverted use of manure is of prodigious importance to agricultural India. The people should be instructed as to what plants to grow for firewood to replace the cow-dung fuel cakes. There is much waste land available as well as the sides of roads and lanes and the edges of the crop fields. There are 2,500 species of woody shrubs and 2,500 species of trees in India. The highly trained experts of the Imperial and Provincial Forest Departments could formulate a scheme for the cultivation of plants for fuel to replace the priceless cow-dung required for crop and pasture land, and initially they might provide the seed for the purpose. It will require much propaganda to bring this about; the use of *uple* has gone on since Indian history began, but it is imperatively necessary that the present diversion of the natural food of the soil should cease; the waste of the manure of over 200 million animals (bovine and equine) is a lamentable loss.

Animals that eat and destroy human food.—Other animals give rise to great economic loss—the monkey, *nilghai*, squirrel, jackal, porcupine and flying-fox interfere with orchard farming to an extent that few know. These animals destroy much that would help to raise the standard of living. Orchard farming should be one of the most popular forms of agriculture. A cheap and abundant supply of fruit and vegetables is one of the best guarantees of good health for all people. Once monkeys or other of these destructive creatures take possession of a garden, there will be little left. Through sentiment the fruit and vegetable grower refuses to take steps to keep down these animals. The result is that in a country in which a large variety of fruit and vegetables can be cheaply grown millions suffer in health because they cannot get them.[2]

Uneducation.—*Want of education* is a solid hindrance to hygienic progress. This is no myth. The 1911 census showed that, of the men, about 17 millions could read and 143½ millions could not; and of the women, only $1\frac{0}{10}$ millions could read, while over 151 millions could not. Public health work in India is probably much younger than many are disposed to believe. It can never take solid root until the people make it part of themselves, and this cannot happen until there is a rise in the number of the educated and in the standard of education in the masses—one of the greatest needs of India is education.

Indebtedness.—The *indebtedness of rural India* to money-lenders is notorious. "There are in some districts whole villages in which every cultivator is in debt; the interest is never under 30 per cent. per annum." Frequently the cultivators' produce is mortgaged to the *bania* on the latter's terms.

[1] *The Pioneer Mail*, September 25, 1925.

[2] From *Proc. of the Meeting of the Board of Agriculture in India, Bangalore*, January 21, 1924.

One of the great mainstays of the rural population at present is the *Co-operative Societies' Movement.* It not merely provides money on easy terms to millions of people. It constitutes a serious educational effort, teaches the people to act together for the common welfare, and shows them how to take part in practical affairs on a broad basis. It is a comprehensive, organic, educative measure. Its potentialities for the good of the people are almost unlimited. It can help to introduce agricultural improvements, press forward education and industry, and create methods of distributing and marketing products. The amount saved to the cultivators annually by the Co-operative Societies and Banks comes to a very large figure ; through them many thousands of mortgaged small-holdings have been redeemed, millions of the people have been freed from the merciless talons of the money-lender, and a real increase in the material prosperity of large numbers of villagers has taken place. Nevertheless Co-operative Societies have not yet fully succeeded in gaining the support and confidence of the people in many parts of India. It seems desirable that the reasons for this want of faith should be inquired into, and steps taken to remove it. Conducted with soundness and integrity, Co-operative Societies are capable of altering for the better the whole aspect of the peasant's life. These Societies have undertaken a herculean task, and are doing splendid work for the unfortunate cultivators ; every possible effort should be made to multiply these highly laudable institutions. The consequences of the indebtedness of rural India are expressed in terms of want, pain, suffering and oppression. "Rural indebtedness and illiteracy together reduce a large number of people to a condition that is practically slavery."

It is curious that the educated youth of India have not had their attention drawn to the profitable avenues of agricultural pursuits. This contrasts remarkably with what is happening in Great Britain. During the last five years the writer has been brought into contact with several young Englishmen and Scotsmen, fresh from taking their Arts degree at Oxford, Cambridge, Edinburgh, Glasgow and Aberdeen, who were going to do two years' training "on the land" to learn scientific farming. There are hundreds of university men all over the country running farms. Men of experience in agriculture maintain that "the diversion of a proportion of the rising generation of the educated class of Indians to the soil would help materially in the agricultural regeneration of India." [1] Not only so, but it would be a profitable pursuit. At present this class seeks to enter the professions which are overcrowded, or Government employment in which the vacancies are limited. It is possible that the introduction of a degree in agriculture in the Indian universities would stimulate them to adopt cultivation of the soil as a career. It is also desirable that Provincial Governments should encourage the establishment of institutions of farming, animal husbandry and dairying, and grant diplomas of efficiency to those who pass through them.

Importance of agriculture.—Compared with agriculture, the other industries of India, though they play a useful part in the economic life of the country, are of minor importance. Agriculture is, and always will be, the great field of industrial activity, for upon it the welfare and prosperity of the large masses of India depend.

The chief cause of India's agricultural backwardness is want of knowledge in her own industry. One remedy for this is elementary education in agriculture, suited to the requirements of the small agriculturist and agricultural labourer and given in village schools for the sons and daughters of these classes. There is little use in providing the best possible seed grain if it is to

[1] *The Pioneer Mail,* November 20, 1925.

be sown in a poor soil which rarely receives manure or artificial fertilisers to feed the crop. Algeria, a pestilential malarious region eighty years ago, "has become a reasonably healthy one of intensive cultivation with scarce room for another blade of grass."[1] The change has led to the view in France that the best way to exterminate malaria is to improve well-being, and good administration can pre-eminently effect this.

Although Agriculture is now a transferred subject, there is abundant reason for the Central Government maintaining its own research laboratories and experimental stations and co-operating with the Agricultural Departments of the Provinces, just as is done by the Federal Government of the U.S.A., which co-operates with the various States of the Union in agricultural propaganda, investigation and education. "There is an enormous field before an all-Indian organisation, which would be in a position to assist the Provinces materially in many ways to stimulate general interest in agriculture. It is a good omen for India that both the Viceroy and the present Secretary of State are determined that there shall be an extension, and a far-reaching extension, of the activities of the Agricultural Departments. An all-India organisation is necessary to achieve the desired end. The field open is an enormous one, and the possibilities almost beyond conception."[2] The economic amelioration of rural India by broad-minded administration will prove a most potent, effective and comprehensive measure in the prevention of malaria.

Arrangement by the agricultural departments of practical demonstrations on the cultivators' own fields is essential to progress, as are also the production and distribution of high-class seed grain on a large scale: individual ryots have to be taught what to do, and the means of doing it must be brought to their door. These departments have demonstrated to the cultivators that the variety of wheat known as "Pusa 12" yields 28 maunds to the acre, twice what the ryot gets out of his crop, and this 28 maunds is of improved quality.

Excellent foundations are being laid and progressive expansion of what is being done by the Provincial Agricultural Departments will produce results that will surprise the people themselves within the present generation. Crores of rupees have been added to the annual wealth of India by the introduction of improved crops alone. In 1924 "there were 5,000,000 acres of land under improved crops, and taking the average of Rs.10 an acre as representing the increased value of the crops, there was an increase of 5 crores of rupees in the value of the crops to the ryots."[3] This is a cautious estimate. A few examples may be given. The standard yield of *gur* from sugar cane in the United Provinces is 1 ton to the acre, but the combination of good cultivation, reasonable manuring and improved varieties has raised the yield to 3 tons; in some instances 4 tons have been attained. Again, in Bihar, a proper system of manuring for rice has given an increased profit to the cultivators ranging from Rs.10 to Rs.50 an acre. The agricultural departments in all provinces have been doing splendid work. In one province this department is demonstrating on 80,000 acres of private land; it is distributing all the good seed it can produce. A huge development of private seed farms and seed stores is much to be desired. Here is one direction in which zamindars can help immensely—distribution of approved seed free to the cultivators; this would educate the farmer in using his own knowledge and experience. It is essential to concentrate energies in teaching the ryot how to make the most of his land.

[1] *The Lancet*, October 31, 1925, p. 927.
[2] *The Pioneer Mail*, September 25, 1925.
[3] The details of this estimate may be found in the *Report of the Agricultural Department* for 1924.

But the generalised introduction of improved seed, proper manuring, iron ploughs, and other requirements of modern agriculture will not be easy and will require organised, continuous, intensive propaganda from village to village, year in year out. Agricultural improvement in India is still young, but it is full of hope. An intensification of the methods now being adopted should, within the present generation, greatly alter for the better the economic conditions of the rural people, if they take advantage of the opportunities now being placed at their disposal. Such progress, however, demands the highest organising skill and the continuous effort of agricultural experts for many years. If, side by side with this improvement, more direct anti-mosquito and anti-malarial measures are adopted, malaria may, in time, become one of the minor maladies of the country.

Lt.-Col. A. ALCOCK, C.I.E., F.R.S., states[1]: "It is to improvement in general sanitation, with no thought of mosquitoes or plasmodia, that the disappearance of malaria from England must be attributed." The change is mainly due to two outstanding items of sanitary improvement that seem to have worked together—namely, drainage and generally improved housing. Improved housing comes with prosperous agricultural conditions. Improve the social and economic conditions, standard of living and sanitation in malarial countries and the malaria vanishes. Its disappearance is accelerated by the various measures referred to in this volume. It is of the utmost importance that the social and economic conditions of the people should be improved, and it is very desirable that this fundamental aspect of the whole malaria question should be appraised.

"The work of the Imperial and Provincial Agricultural Departments is one of the brightest pages in the modern history of our administration in India."[2]

Ultimate effects of canal irrigation.—Sanitarians in India have railed against inundation and flooding by rivers, knowing that when these floods are drying up malaria follows, but forgetting that these inundations enrich the soil and are responsible for the abundant crops that follow. It is the floods of France, Italy and other countries in Europe that have enabled the farmers to produce the heavy crops that have been the source of their prosperity and many of the amenities of their present civilisation, which, *inter alia*, have enabled them to overcome the onslaughts of malaria. If we review the areas in India and Burma subject to inundations, we will find that they are the regions of the greatest prosperity. The only exception to this is the flooded areas of the Punjab, which are periodically subjected to decimating malaria, regarding which we know little at present. On the other hand, if we consider the areas where irrigation canals are in operation, we find that there is not only malaria, but, if the soil is not properly manured, there is a gradual deterioration in the fertility of the soil because the water does not give to the land the enriching film of silt that is so valuable to the crops. Hence the urgent necessity that all irrigated land should be provided with some form of fertiliser, whether it be animal or artificial manure. It is the want of such fertilisation that is converting much of this land into a barren alkaline waste. This is a subject that requires most serious consideration and further investigation.

Whilst a great deal of improvement has taken place in limited areas in India, only a fraction of the more remote parts of the country has been touched. In the depths of the rural districts there is little sign of scientific farming—the modern plough and drill are unknown and little manure nourishes

[1] "The Anopheles Mosquito in England," *The Lancet*, July 4, 1925, p. 34.
[2] *The Pioneer Mail*, October 30, 1925.

the crop. Many districts still depend for crops on the rain, others on wells with hand- or bullock-drawn water.

The writer feels that for years to come the main stimulus for agricultural improvement must emanate from Government, but earnestly hopes that a progressively increasing number of educated patriotic Indians will participate energetically in the work of rural regeneration. On the whole he believes that an era of prosperity is coming to India, unless she wantonly turns her back on the gifts of the gods. It is not coming from her mineral resources, but from the sweat of the brow of her rural population. He says no more lest his words may be considered the exaggerations of an idle dreamer. That is the time when the anti-malarial sanitarian will come into his own. It is highly probable that the writer will not live to see this gratifying millennium, but that it will occur in the present generation, if full use is made of the opportunities that will arise, he has no doubt whatever.

An improved economic state is indissolubly bound up with the question of the food of the masses. The one-sided, badly balanced diets in general use, deficient in nutritive elements and vitamins, lead to many diseases, including scurvy, epidemic dropsy, beri-beri, chronic debility, loss of stamina, lowered vitality and decreased resistance to disease generally. A defect in diet is the widespread use of polished rice; it is a fruitful source of physical degeneration and loss of tone. Fruit and vegetables in abundance, and a good supply of pure milk, are much wanted in the Indian's diet. It has been previously stated that immunity from malaria can be developed, and an adequate quantity of suitable food is an important factor in the acquisition of this immunity; a healthy body is the best defence against malaria, and a sufficient diet of suitable material is the best means of maintaining the body in health.

A *progressive anti-malarial policy* in rural areas would have to provide for improvement of many of the existing conditions, for legislation dealing with the circumstances favourable to the spread of malaria, including statutory obligation on the individual to protect himself, his dependents, and employees, and for anti-malarial work as an essential feature of every land settlement, irrigation, educational and relief scheme; and it would attach the greatest importance to the economic and social factor. The amelioration of the conditions of life of cultivators has in many malarial countries contributed to raise the standard of individual vitality and resistance to malaria among people liable to contract malarial infection. The movement for the formation of co-operative anti-malarial societies (p. 376) inaugurated by Dr. Rai Gopal Chandra Chatterji Bahadur is full of promise. It is a great conception and a huge task.

It is always with the greatest reluctance that anything is said or written about the religions of India, yet they pervade the whole atmosphere—social, educational, hygienic, agricultural and political. At every turn the sanitarian is hampered by custom and caste under religious rule. Caste may be social custom, but it had its origin when Brahmins claimed that they were much better than other people. If the public health officer inveighs against prevailing insanitary or unhealthy practices, he is declared to be interfering with religious freedom. The health officer is perpetually fighting against long odds. The writer speaks from experience—he was health officer of one of the largest municipalities in India for ten years. Caste restricts the free movement and utilisation of labour, maintains the deplorable conditions associated with the existence of an enormous class of untouchables, and prevents the utilisation of waste products.

It is with some hesitation that the writer introduced the melancholy subject of the social and economic condition of the masses of India. He would have been wanting in candour were he to have omitted it, for he

feels profoundly that the prevention of malaria in India is most intimately connected with, probably inseparable from, improvement in the economic condition of the rural population. The task of solving successfully the rural problem is so highly complex, so overwhelmingly big, and so elusive that many would abandon it. There are thousands of Englishmen, who have spent the best part of their lives in service to India and have an abiding affection for the Indian cultivator, who are filled with revolt at such a counsel of despair. The economists, agricultural administrators, social reformers, and members of the Indian Civil Service are familiar with the subject under reference, and are prepared to help the rural people if they will only help themselves in the ways mentioned. A solution of the rural problem is imperative; to wait until the political current is running more gently is deplorable procrastination. It is a costly undertaking, but the end to be achieved is worth it. Effective dealing with malaria is not simply a matter of doing away with collections of water, filling up or draining borrow-pits and distributing a limited amount of quinine. To produce a material reduction in the malaria of India is a dream that patient and painstaking men and women working together can convert into a glorious reality. Lowering the incidence of rural malaria is the great problem of India, and because it is bound up with that of improving the economic and hygienic state of the rural masses a brief consideration, though incomplete and imperfect of the latter had to be included in this volume.

APPENDIX I

MALARIA STATISTICS OF INDIA FOR 1924

(See pp. 9–16)

The following Tables [1] give the latest available statistics in connexion with malaria in India. They supplement those given on pp. 9–16.

ADMISSIONS AND DEATHS FOR MALARIA IN THE ARMY IN INDIA IN 1924

a. BRITISH TROOPS

Admissions and Deaths by Commands [2]

Command.	Admissions.		Deaths		Case mortality per cent.
	Actuals.	Ratio per 1,000.	Actuals.	Ratio per 1,000.	
Northern	6,584	400·5	6	0·37	0·1
Waziristan District	575	340·0	—	—	—
Eastern	2,345	153·1	5	0·33	0·2
Western	620	120·9	1	0·20	0·2
Southern	1,724	101·7	1	0·06	0·1
Aden Brigade	134	99·0	1	0·74	0·7
Troops on the line of march	45	88·4	—	—	—
Burma District	93	49·9	—	—	—
All India	12,120	206·8	14	0·24	0·1

The admissions and deaths for malaria in 1924 were 206·8 and 0·24 per 1,000, respectively, as compared with 172·2 and 0·27 in 1923. Malaria continues to be the dominant cause of admission to hospital, "and it cannot yet be said that any real measure of control has been obtained." [3]

"Schemes have been drawn up for all malarious stations and are in operation to the extent to which funds will permit. It is hoped also that as a special measure *additional funds may be obtained for mosquito-proofing* the barracks at some of *the worst stations.*" The writer would strongly urge this being done; he did so in 1914 when acting as D.D.M.S., A.H.Q., India.

[1] From the *Report of the Public Health Commissioner with the Government of India* for the year 1924, Vol. I.
[2] *Ibid.*, p. 160.
[3] *Ibid.*

CLASSIFICATION OF THE ADMISSIONS FOR MALARIA IN 1924

The actual admissions for all India in 1924 were 12,120:

Fresh infections—4,515 cases

Benign tertian	3,273
Malignant tertian	768
Quartan	21
Mixed infections	13
Diagnosed clinically	440
TOTAL .	4,515

Relapses.—7,605 cases

Benign tertian	6,133
Malignant tertian	661
Quartan	9
Mixed infections	15
Diagnosed clinically	769
Malarial cachexia	18
TOTAL .	7,605

Ninety per cent. of the cases were accurately diagnosed by microscopical examination of blood films, the remaining 10 per cent. being diagnosed on clinical grounds.

b. INDIAN TROOPS

ADMISSIONS AND DEATHS BY COMMANDS

Command.	Admissions		Deaths.		Case mortality per cent
	Actuals	Ratio per 1,000.	Actuals.	Ratio per 1,000.	
Troops on the line of march .	200	517·9	—	—	—
Aden and Bushire .	527	270·8	2	1·05	0·38
Waziristan District . .	3,349	182·5	16	0 87	0 48
Northern . . .	7,114	157·4	20	0 44	0·28
Eastern . .	2,669	120·2	5	0·23	0·19
Burma District .	464	111·5	7	0·08	1 51
Southern	1,867	80·8	6	0·26	0 32
Western . . .	1,242	63·8	3	0 15	0·24
ALL INDIA .	17,432	129·4	59	0·44	0·34

Malaria is still the outstanding disease, causing almost one-third of the total sickness among Indian troops. The figures for 1924, however, show an improvement over those of any year since the quinquennial period 1910–14; there was a fall of 28·7 per 1,000 in the admission compared with 1923. This improvement, in spite of heavy and late rains in the autumn of 1924, may be partly attributed to the provision of mosquito nets, which are now part of the sepoy's personal clothing.

CLASSIFICATION OF ADMISSIONS FOR MALARIA IN 1924

The actual admissions for all India in 1924 were 17,432.

Fresh infections.—3,293 = 18·89 *per cent of total cases*

Benign tertian	1,849
Malignant tertian . . .	849
Quartan	5
Mixed infections	17
Diagnosed clinically	573
TOTAL .	3,293

Relapses.—14,139 = 81·11 *per cent. of total cases*

Benign tertian	6,121
Malignant tertian	2,496
Quartan	14
Diagnosed clinically	4,958
Malarial cachexia	522
Mixed infections	28
TOTAL .	14,139

CIVIL POPULATION

TABLE OF CASES OF MALARIA TREATED IN HOSPITALS AND DISPENSARIES IN BRITISH PROVINCES IN 1924 [1]

Province.		State, Public, Local Fund and Private aided Dispensaries		State, Special and Railway Dispensaries		Private non-aided Dispensaries.	Total.	
		Indoor	Outdoor.	Indoor.	Outdoor			
Bengal . .	1923	6,657	1,595,849	8,230	140,627	384,571	2,135,934	1923
	1924	6,738	1,385,414	7,195	144,150	325,345	1,868,842	1924
Punjab . .	1923	7,209	953,903	3,340	214,402	17,823	1,196,677	1923
	1924	7,692	1,047,349	4,101	240,190	16,332	1,315,664	1924
Madras . .	1923	8,369	528,406	953	36,825	36,724	611,277	1923
	1924	10,680	591,470	862	22,755	32,502	658,269	1924
Assam . .	1923	2,422	203,145	2,381	26,558	9,140	333,646	1923
	1924	2,360	296,081	2,171	25,312	6,463	332,387	1924
Bihar and Orissa	1923	3,624	719,302	2,553	80,577	126,452	932,508	1923
	1924	3,527	914,285	2,429	77,339	141,425	1,139,005	1924
Central Provinces	1923	2,324	239,079	1,191	49,458	34,578	326,630	1923
	1924	2,446	236,307	936	41,813	39,372	320,934	1924
United Provinces .	1923	5,540	845,702	5,629	88,445	68,554	1,013,960	1923
	1924	6,176	1,083,708	9,448	112,053	106,567	1,318,042	1924
Bombay . .	1923	7,158	434,088	5,141	81,746	231,149	759,582	1923
	1924	8,393	527,989	4,931	88,669	233,860	803,842	1924
North-West Province .	1923	1,645	187,472	5,403	53,195	7,872	255,587	1923
	1924	1,697	184,369	6,282	53,848	6,006	252,102	1924
Burma . .	1923	13,468	239,823	6,709	31,414	Nil.	291,414	1923
	1924	14,040	225,459	5,452	32,092	Nil.	277,043	1924
TOTAL .	1923	58,122	6,036,859	41,530	803,247	917,163	7,857,221	1923
	1924	63,749	6,492,581	43,807	838,221	907,772	8,346,130	1924

This Table supplements that given on p. 13. On the whole 1924 was not a bad malaria year, although there were nearly half a million more cases treated under observation in the civil population than in the previous year. The Provinces of Delhi, North-Western Provinces, Assam, Central Provinces and Burma have shown decreases as compared with 1923; the rest have recorded increases.

MORTALITY FROM MALARIA IN INDIA

(See p. 15)

As remarked on p. 15, it is still not possible to state the true death-rate from malaria in India. Laudable efforts are being made by the medical statistical authorities to reach something approaching accuracy. "From various verification data a

[1] From the *Report of the Public Health Commissioner with the Government of India* for the year 1924, Vol. I, p. 30.

correction factor has been evolved for fever mortality which approximately places about one-third of the deaths returned under 'Fever' as being due to true malaria. This figure must needs vary in different provinces under different epidemiological conditions when variations in excess or defect might be very considerable. Directors of Public Health of the United Provinces and of Bihar and Orissa consider the error is much greater in their provinces. As a working rule, however, one-third to one-fifth may be taken as a fairly true average."[1]

Of the 8,346,130 cases treated in Government hospitals and dispensaries in 1924 there were 4,007,662 deaths from "fever," giving 1,335,887 due to malaria. This represents but a small fraction of the 80 to 100 millions of cases of malaria that occur in the Indian Empire annually. "Only thus can we view in their true perspective the problems of treatment and prophylaxis by quininisation, the prohibitive costs, and the difficulties of supply."[2]

[1] *Report of the Public Health Commissioner with the Government of India* for the year 1924, Vol. I, p. 30.

[2] *Ibid.*, p. 31.

APPENDIX II

THE MALARIA MAP OF INDIA

(See p. 16)

THIS MAP, as stated in the text (p. 16), was originally prepared for the present volume at the Central Malaria Bureau, Kasauli, under the skilful direction of Lt.-Col. S. R. CHRISTOPHERS, C.I.E., O.B.E., F.R.S., I.M.S. The block of the Map, as it appears in this book, was prepared by the Oxford Medical Publications Press from the original sent to the author by Lt.-Col. CHRISTOPHERS in 1924.

The writer is indebted to the *Ind. Jour. Med. Res.*, Vol XIV, No. 1, July 1926, and the *Annual Report of the Public Health Commissioner with the Government of India* for the following explanatory note by Lt.-Cols. S. R. CHRISTOPHERS and J. A. SINTON, V.C., O.B.E., D.Sc., I.M.S., regarding the colour scheme of the Map.

"The map has been coloured to display the major epidemiological features of malaria in India so far as they are at present known and capable of being mapped by variations in endemicity.

"The more fundamental epidemiological aspects of malaria distribution, *i.e.*, the division of India into tracts where malaria prevalence is liable to be seasonal and epidemic and those where malaria is more perennial and endemic, are shewn by pink and blue tones, respectively.

"In pink tones are exhibited all those extensive tracts where, owing to climatic and physical conditions (sub-tropical semi-desert zone), malaria prevalence is markedly seasonal in character, and where malaria endemicity is low or moderate, except when and where special conditions cyclical, seasonal or local lead to its enhancement. A high spleen rate when present in such areas is, as a rule, either the result of abnormally heavy monsoon rainfall (epidemic tracts) or of the existence of special local conditions favouring the disease such as neglected irrigation, water-logging, etc.

"Within the light pink area are indicated in a darker shade of red the areas in this zone known to be liable to the epidemic malaria characteristic of this part of India (so-called 'autumnal,' 'fulminant' or 'diluvial' malaria of Christophers and Gill). These epidemics are pandemic in character, usually occurring at intervals of about eight years and affecting enormous tracts up to 10,000 square miles or more in extent. They exhibit in a marked degree a *focal* distribution and can be mapped by lines of equal mortality (isothans), when they shew contour-like zones of increasing intensity as the centre of the disturbed area is approached. They resemble in a greatly exaggerated form the normal autumnal increased prevalence of malaria in these parts, and are displayed in the statistics by a very characteristic seasonal epidemic curve easily differentiated by its time of occurrence and by the shape of the graph from mortality curves due to any other disease. In the heart of the epidemic, villages and small towns are alike visited as by a pestilence, the mortality over hundreds of square miles rising during the prevalence of the epidemic (from late September to December) to 400 per mille or more, so that for this period the death rate may be 10, 20 or even 30 times the normal.

"The spleen rate during the epidemic rises from a low figure to 80 or 90 per cent. and then gradually falls again through a period of some five years until it once more reaches the normal low figure. The mortality, but not necessarily the morbidity, is preponderatingly among infants, young children and the aged. Should a given tract be unfortunate enough to come within the zone of influence of two or more such epidemics in the decade the population figure in the next census may fail to exhibit the normal increase or shew a decrease of population.

"The epidemics are the result, under certain circumstances, of unusually heavy rainfall and there is no doubt that they are largely dependent on extensive diluvial conditions resulting from abnormal rainfall upon river drainage systems normally unaccustomed to cope with such precipitation. From the map it will be seen that the chief site of election for such manifestations is the submontane plain of the Punjab, but less extensive manifestations may occur in Sind and elsewhere in the zone coloured light pink on the map. As a result of knowledge of the causation of these epidemics much attention has been given by the Government of the Punjab to the control of flooding in the dangerous areas, and since no major epidemic comparable to those of 1890–1901 and 1908 has recently occurred this may have had a deterring effect. By the aid of prompt report of meteorological data Gill has been able to make very accurate annual forecasts of liability of particular areas in a given year to this form of malaria, thus enabling early steps to be taken in respect to quinine distribution and other ameliorative measures.

"As will be clear these vast cyclical disturbances form a problem altogether special to this part of India and it is important that their potential zone of action should be indicated on the map. The areas depicted are such as have at least once shewn a mortality of 10 times the normal death rate during an epidemic (*see* pp. 50, 51).

"Apart from the temporary effect of epidemics of the above character (post-epidemic hyper-endemicity) a raised endemicity of malaria within the areas marked light pink is most frequently associated with irrigation, more especially with old defective systems where leakage and water-logging are a feature. Such areas of raised endemicity are, however, usually limited in extent. Very rarely even here is the spleen rate comparable to that in the so-called hyper-endemic tracts described later, and such high endemicity is seldom associated with the relative adult immunity so characteristically seen in the true hyper-endemic areas. To the north of the area of marked seasonal enhancement there exist, as indicated on the map, submontane areas where the endemicity may be permanently high, associated with hill streams, etc.

"In light blue tones are indicated those extensive portions of India where, owing mainly to climatic and physical conditions (humid semi-tropical or tropical areas), malaria is much more stable in its manifestations. Here rainfall is both heavier and its excess less associated with enhanced incidence of malaria.

"In areas coloured light blue are depicted those extensive and varied tracts in which malaria through innumerable towns, villages and hamlets[1] occurs in varying degrees of intensity, practically never absent and correspondingly prevalent where local conditions are favourable.

"Malaria here is largely a reflex of a multiplicity of natural features of the country, rainwater collections, streams and rivers, swamps, ponds and lakes (tanks). In addition ricefields and irrigation play their part. On the whole, throughout the areas coloured light blue the endemicity is moderate to high, though areas of very low endemicity with a spleen rate under 10 per cent. (healthy areas) are common. Some known healthy areas are depicted on the map in light green; but insufficient is known at present as to the extent or permanence of such areas to make their mapping in detail possible. It is perhaps worth mentioning that some of the known healthy areas of this kind are not to any noticeable degree free from anophelines and that they may be, and in fact usually are, associated with extensive rice culture.

"Within the light blue zone are shewn in darker tints those tracts which it has been customary in India to refer to as *hyper-endemic tracts*. In the hyper-endemic tracts the spleen rate is consistently and permanently high, rarely under 50 per cent. and frequently 90 per cent. or over. Such areas of raised endemicity frequently have sharply defined limits, so that passing beyond these the spleen rate, often within a few miles, changes abruptly from the high values universal in the hyper-endemic tract to low or moderate values characteristic of more healthy areas adjoining. In the more typical areas of this kind the high spleen rate in children (spleen rate) is associated with a relatively low rate in adults (adult spleen rate), and the adults also

[1] NOTE.—There are in British Administered India alone approximately 200,000 villages and towns of over 500 inhabitants and 500,000 villages and hamlets with under this number.

shew considerable immunity to malaria and suffer little from its effects. Depending upon circumstances, however, there may be a high rate also in adults and in all cases non-immune immigrants show a high malarial incidence. Non-immunes visiting such an area are extremely liable to contract malaria, often of a severe type, and Europeans and others of susceptible race resident in the area suffer constantly from malaria.

" In dark blue are represented known hyper-endemic areas, where the hyper-endemicity is associated with and appears to be an essential feature of low jungle or forest-clad hills (1,000 to 3,000 feet altitude) or terai country (footslopes of higher hills). This association of hilly country with enhanced malarial endemicity is one of the most marked and invariable features of malarial epidemiology in India, more especially in the south and east. Most of the notorious ' unhealthy ' tracts are of this character and it is such areas which constitute the known endemic foci of black-water fever, the only essential for such a focus within a hyper-endemic tract of this kind being the presence of resident Europeans or other susceptible race. As a rule such areas, though extensive, are wild and jungly in character and populated by primitive aboriginal races who, beyond a universal infection in childhood, exhibit but little evidence of the disease. It is only where industrial enterprise (tea planting, forestry, mining, etc.,) is attempted that the full potentialities of such areas are made fully apparent. Among better known areas of this kind may be mentioned the Sigur Ghât (referred to in Ross's earlier work), the Darjeeling Terai and the Duars, the Nepal Terai, the Jeypore Hill tracts and the forests of Singhbhum.

" In purple are shewn hyper-endemic tracts not of this nature. Conspicuous among such is the extensive area of high endemicity studied by Fry, Bentley and others in the plains of Bengal. Here hyper-endemicity is apparently associated with secular changes affecting the physical conditions (decayed rivers) and indirectly also through diminished fertility of the soil and loss of trade, etc., the economic prosperity of the population.

" Smaller areas of local hyper-endemicity seem in some localities to arise as a result of a slow enhancement of malaria through a period of years (epidemic malaria of tropical tracts); one such area formerly reputed healthy but later notoriously malarious is indicated on the map on the coast north of Madras City (Ennur, etc.).

" A purple colouring of the Andaman Islands serves to call to attention almost the only known example in India of that form of high endemicity associated with *A. ludlowii* and a coastal distribution of malaria, which though almost non-existent in India, except possibly in some parts of Burma, constitutes further east through thousands of miles of coast in the Dutch East Indies perhaps the most important form of malaria in these parts.[1]

" Lastly mention should be made of areas which by reason of altitude above sea level are either entirely free from malaria or so relatively free that they shew no definite endemic or epidemic prevalence. Roughly speaking, in India tracts or localities of 5,000 feet altitude or over come within this category, but under special circumstances (Quetta) malaria may occur and even be prevalent at this height. Such malaria-free areas are indicated in yellow on the map."

[1] See pp. 109, 110 and 329

APPENDIX III

ANTI-MOSQUITO LEGISLATION

ANTI-MOSQUITO BY-LAW FOR THE PREVENTION OF MOSQUITO-BREEDING IN MUNICIPALITIES[1]

(See p. 240 *et seq.*)

The following is suggested as an anti-mosquito ordinance suitable for municipalities. Some such by-law has been introduced into the cities, towns and villages of several malarious countries, and has been found to work satisfactorily.

1. It shall be unlawful to have, keep, maintain, cause or permit within the limits of . . . . . . any collection of standing or running water in which mosquitoes breed or are likely to breed, unless such collection of water is treated so as effectually to prevent such breeding.

2. Any collections of water considered by Clause 1 of this by-law shall be held to be those contained in ditches, pools, ponds, excavations, holes, depressions, fountains, tanks, shallow wells, cisterns, open cesspools, cesspits, troughs, barrels, chatties or *gurrahs, naunds*, kerosene oil tins, tubs, cans, buckets, defective house-roof gutters, bottles, and domestic water containers of all descriptions, tanks for flush closets, and other similar water containers.

3. The method of dealing with any collections of water specified in Clause 2, for preventing the breeding of mosquitoes, shall be approved by the Municipal Corporation [or Health Officer, or Malaria Officer, or other official appointed by the Municipal Corporation] and may be any one or more of the following :

(*a*) Screening with wire gauze netting of at least 14 to 16 meshes to the inch each way, or with any other material which will effectually prevent the ingress and egress of mosquitoes.

(*b*) Complete emptying every seven days of unscreened containers, together with their thorough drying and cleaning.

(*c*) Using a larvicide approved by the Health Officer [or Malaria Officer, or other official appointed by the Municipal Corporation].

(*d*) Covering completely the surface of the waters with kerosene, petroleum, or a mixture of heavy mineral oil, kerosene and country castor oil (or other approved larvicide) once every seven days.

(*e*) Cleaning and keeping sufficiently free of vegetable growth and other obstruction [and stocking with mosquito-destroying fish [2]].

(*f*) Filling or draining to the satisfaction of the Health Officer [or Malaria Officer, or other official appointed by the Municipal Corporation].

(*g*) Proper disposal by removal or destruction of tin cans, tin boxes, broken or empty bottles and similar articles likely to hold water.

4. The natural presence of mosquito larvæ in standing or running water shall be evidence that mosquitoes are breeding there and failure to prevent such breeding within three days shall be deemed a breach of this by-law.

5. Should the person or persons responsible for conditions giving rise to the

[1] Modified from an Ordinance of the U.S. Public Health Service and the International Health Board as quoted in HARDENBURG'S *Mosquito Eradication*.

[2] Omit if such fish are not available.

breeding of mosquitoes fail or refuse to take the necessary measures to prevent the same, within three days after due notice has been given to them, the Health Officer [or Malaria Officer, or other official appointed by the Municipal Corporation] is hereby authorised to do so, and all necessary cost incurred by him for this purpose shall be a charge against the owner or other person offending, as the case may be.

6. For the purpose of enforcing the provisions of this by-law, the Health Officer [or other official duly appointed by the Municipal Corporation, acting under their authority] may at all reasonable times enter in and upon any premises within his jurisdiction [1]; and any person or persons charged with any of the duties imposed by this by-law failing, within the time specified by this by-law, or within the time stated in the notice of the Health Officer, as the case may be, to perform such duties, or to carry out the necessary measures to the satisfaction of the Health Officer, shall be deemed guilty of a breach of this by-law.

7. *Any person who shall violate any provision of this* by-law shall *on* each conviction be subject to a fine of not less than....... ....or more than ...., in the discretion of the court.

8. All by-laws or parts of by-laws in conflict with this by-law are hereby repealed and this by-law shall be in force and effect...................days after its passing into law.

Passed this....................day of............

[1] In most municipalities of India, in the case of certain castes, it is necessary to give due warning of such proposed entry.

APPENDIX IV

(See p. 392)

LEAFLET ON THE CAUSES AND PREVENTION OF MALARIAL FEVERS

Malarial fever is due to parasites in the blood. There are two kinds of cells in the blood, red and white. Malaria parasites attack the red cells.

These parasites are carried from man to man by certain kinds of mosquitoes. The two chief kinds of mosquitoes are called *Anophelines* and *Culicines*. Anophelines are the malaria-carriers. Nearly all Anophelines, when resting on a wall, hold their bodies at an angle to it; the head, proboscis (the biting mouth parts of a mosquito) and body are in a straight line, and the insect looks like a small thorn stuck slanting in the wall. Culicines rest with their bodies parallel with the wall and appear as if hunchbacked. The colour of anophelines is light or dark brown, of culicines grey, brown or black with white bands or markings. In anophelines the wings are spotted; in culicines the wings are plain.

Anophelines, like all mosquitoes, breed in water. In water they lay eggs, the eggs hatch, and larvæ are set free. The eggs of anophelines can only just be seen in water, in which they float singly; the eggs of most culicines occur as little boat-shaped masses, those of others float singly.

Mosquito larvæ are called "wrigglers" from the way in which they move. The larvæ of anophelines are easily known by their lying flat on the surface of the water, and by their moving backwards in jerks; culicines hang in water head downwards from a long breathing tube, and move forward with a wriggling motion.

About a fortnight after the eggs of anophelines are laid the full-grown mosquitoes are formed and fly away. If houses or huts are near, they enter and feed on man's blood. If the blood contains malaria parasites, these undergo changes in the anophelines and ten days later, if the mosquitoes bite a healthy person, that person gets malarial fever.

Anophelines may breed in any collection of water in houses, pools outside houses, in cisterns, drains, tanks, wells, canals, streams, rivers and water channels of all kinds, chatties, barrels, kerosene oil and other tins, and bottles. Hence it is very important to prevent mosquitoes getting at the water in or near houses by keeping water vessels covered, and to avoid all unnecessary collections of water near houses; any articles that can hold water, such as old and broken chatties, kerosene oil tins, broken bottles, etc., should be cleared away. Keep your yards and compounds free from stagnant water of all kinds. All pools near houses should be abolished by filling up the holes in which they occur. When pools cannot be filled up, a little kerosene oil (about a large tablespoonful for a square yard of surface) should be thrown on the surface of the water once a week; this will kill all mosquito larvæ. It is wise to try and kill all mosquitoes found in houses. Sleep under a mosquito net. Cut down useless scrub and jungle around your house.

Quinine will usually kill any malaria parasites that get into the blood. A small dose of quinine every day during the malarious season will, in most people, prevent malarial fever altogether. When malarial fever occurs large doses cure it, but to be certain of killing all the parasites in the blood it is necessary to take a dose daily for three months. Nearly all children in India have malaria parasites in their blood, and most children have enlargement of the spleen due to these parasites. All children who

get malarial fever, and all who have enlargement of the spleen, should be given quinine every day for three months. This will usually cure them of malaria.

During the malarious season everyone should take quinine regularly to prevent malarial fever.

THIS LEAFLET, OR SOME MODIFICATION OF IT, SHOULD BE PRINTED IN LARGE NUMBERS AND PERIODICALLY DISTRIBUTED, SAY TWICE A YEAR, SO THAT THE MAIN FACTS CONNECTED WITH MALARIA AND ITS PREVENTION ARE KEPT CONSTANTLY BEFORE THE EYES OF THE PEOPLE. IT WOULD BE IMPROVED BY PICTURES OF MALARIA PARASITES IN THE BLOOD, ADULT ANOPHELINE AND CULICINE MOSQUITOES, THEIR LARVÆ AND EGGS.

APPENDIX V

(See p. 402)

A.—MALARIA SURVEY QUESTIONNAIRE FOR TOWNS, CANTONMENTS AND LIMITED AREAS

MALARIA INQUIRY________________(Place, Town, Cantonment, etc.), 19 .

WHAT anti-malarial and anti-mosquito measures are adopted in and around[1] . . . . . as regards :—[2]

1. Quinine prophylaxis—dose, interval between doses, whether given at definite periods of the year and within fixed dates, or irregularly; date of commencement and date of stopping. Percentage of malaria cases to population when prophylactic issue commenced. What effect has it on the incidence of malaria? Compare this year's results with those of previous years. Is quinine given universally?

2. Are mosquito nets used by the inhabitants—in houses, huts, cantonments, hospitals, etc.? What kind of net is used, and is it efficient? Are electric fans or ordinary punkahs in use? Are the punkahs worked mechanically or pulled by punkah coolies? Is anti-mosquito fumigation practised? If so, how often and in what way?

3. Are anti-larval measures employed? Petrolege in :—Collections of natural surface waters, large and small, artificial collections of water? How is the kerosene (or other larvicide) used? How often is it used? Are domestic collections of water covered with any mosquito-proof material? Is there any jungle, scrub or brushwood around the . . . . . . (town, cantonment, village, etc.)? Are clearing and burning of jungle, scrub and brushwood carried out? If so, how often each year and at what times? Are weeds, grass and water plants cleared from drains, water channels, and small and large collections of open surface waters? If so, when, and how often? Are small excavations filled up and irregularities of the surface levelled? Are any major and minor anti-mosquito works, such as surface drainage, now being carried out? Is a "mosquito brigade" employed? If so, what is the strength of the gangs, are they employed throughout the year, and, briefly, what duties do they carry out? Is any anti-mosquito legislation in operation? If there is, how is it enforced by the municipality (or cantonment committee, etc.)? Are there any irrigation canals in or near the town (or cantonment, etc.); if there are, what effect have they on the subsoil-water level, and the formation of surface pools? How are private gardens in the town (or cantonment, etc.) watered? Are garden cisterns or other containers of stored water for gardens protected from mosquitoes? Give a sketch of all breeding-places of Anophelini in the town (or cantonment, etc.) and within 800 yards of the town (or cantonment, etc.) limits, showing the geographical relationship between those breeding-places and the various adjacent houses (barracks, hospitals, etc.).

4. How are malarial fever cases diagnosed in the hospitals, dispensaries, etc.? Clinically? By microscopic examination of the blood? What is the percentage of admissions for malignant tertian, benign tertian, quartan? What other fevers, if any, are prevalent? Are all cases of diagnosed malarial fever treated in hospital? Are malarial fever cases isolated? If so, in what way? Are there sufficient mosquito nets in the hospitals for all cases of malarial fever? Are the hospitals mosquito-proofed by wire-gauze netting? Are electric fans or punkahs in use in the hospitals? How long is quinine used after the last paroxysm, and how is it continued after the patient

[1] Name the place—town, cantonment, asylum, jail, factory, etc.
[2] Leave space after each question for the answer.

leaves hospital? How long, usually, are patients kept in hospital after the last paroxysm? Do the discharged cases attend hospital for quinine, and if so for how long? *Is a nominal roll of the patients who should attend kept in the hospital?* What proportion of cases of malarial fever are treated as "detained" (military, police, jail and asylum hospitals)?

5. What is the percentage of relapses to fresh infections? Are these relapses the result of last year's local infections, or of infections acquired elsewhere?

6. Give a sketch showing the number and types of malarial fever cases that have occurred in different quarters of the town (or barracks, houses, etc.) and showing roughly whether there is any relation between the infected areas?

7. Have the people acquired any degree of relative immunity?

8. Has the endemic malarial index[1] of the town (cantonment, etc.) been worked out? If so, what is it?

9. Has the general spleen rate, and that of children from 0 to 10 years of age, been worked out? If so, what are these percentages?

10. In the case of Indian troops in garrisons, police battalions and all organised bodies of men:—What are the dates of men going on furlough, and on an average how many go with each batch? For what length of time? Are the men examined on return from furlough? What is the condition of the men as regards malaria on returning from *furlough (enlarged spleen, malarial anæmia, actual malarial fever)? Where are* the Indian homes of the men, and are they in malarious districts?

11. What species of Anophelini have been found in and near the town (cantonment, etc.)? Natural malaria-carriers? Non-carriers? Give a sketch showing the breeding-places of the species of Anophelini found in particular parts of the town (or cantonment, etc.). What time or times of the year do Anophelini appear? What time or times do Anophelini disappear? Are Anophelini found all the year round?

What are the breeding-places of Anophelini within half a mile of the outskirts of the town (or cantonment, etc.)? Give a rough sketch of them. What species of Anophelini ova and larvæ have been found in these places? What breeding-places, if any, are there in the town (or cantonment, etc.)? Give a rough sketch of the breeding-places. What species of Anophelini ova and larvæ have been found in them? What breeding-places, if any, are there in the immediate vicinity of the town (or cantonment, etc.)? What species of Anophelini ova and larvæ have been found in them? Does anophelism occur at any time in the year? If so, when?

Are there any villages in the immediate vicinity and within half a mile of the town (or cantonment, etc.)? If any such exist, is malaria prevalent in them, and to what extent?

State briefly the previous history of malaria in the town (or cantonment, village, etc.).

B.—MALARIA SURVEY QUESTIONNAIRE FOR DISTRICTS, PROVINCES AND LARGE AREAS GENERALLY

1. Has epidemic malaria[2] occurred in the district, province, etc.? If so, in which years? What have been its distribution and intensity in those years? What parts of the district, province, etc., have never suffered from epidemic malaria?

2. If epidemic malaria has occurred, what have been its relations to: (*a*) rainfall; (*b*) physical features; (*c*) social, racial and economic conditions; (*d*) humidity?

3. Which are respectively the:—(*a*) healthy areas; (*b*) moderately endemic areas; (*c*) highly endemic areas; (*d*) hyperendemic areas, in the district, province, etc.?

4. What are the findings as regards nature and extent of breeding-places, species of Anopheles, sporozoite rate, humidity, and economic conditions in particular examples of highly endemic areas or special foci of endemic malaria?

What is the character of the death-rate in those areas, and what is the effect of malaria in regard to (*a*) the age curve of total mortality and the age composition of the population? (*b*) the birth-rate and the prevalence of stillbirths?

[1] Percentage of children from 0 to 10 years of age whose blood contains malaria parasites.

[2] As defined on pp. 16 and 49.

5. To what extent does malaria prevail in the large and small towns as ascertained by careful malaria surveys ?

6. What species of Anopheles occur in the district, province, etc. ? Half a dozen males, and the same number of female Anopheles, should be mounted and sent to the provincial malaria bureau, if possible with larvæ and ova. [In order that the parasites occurring in different parts of India may be compared, it is desirable that specimens from as many areas as possible may be sent to the Central Malaria Bureau, Kasauli.]

7. What is the distribution and seasonal prevalence of the different species of Anopheles occurring in the district, province, etc. ? What are the breeding-places usually selected by the different species ? What species, if any, develop in rice-fields ? Which are the different species concerned in the spread of malaria in nature ?

8. In highly endemic and hyperendemic areas, to what extent are the people infected with malaria parasites, and what is the usual percentage of infected Anopheles ?

9. In highly endemic and hyperendemic areas, what is the proportional prevalence of the different kinds of malaria parasites ?

10. In what parts of the district, province, etc., if any, does blackwater fever occur ?

Many of the points referred to in Questionnaire A also apply to malaria surveys of districts, provinces and large areas generally.

APPENDIX VI

SOME IMPORTANT ITEMS ADDED TO OUR KNOWLEDGE OF MALARIA WHILE THIS VOLUME WAS PASSING THROUGH THE PRESS

1

REPORT ON MALARIA IN THE CENTRAL PROVINCES

(See pp. 40, 41)

THIS Report on Malaria in the C.P., 1912–13, consisting of 191 pages, 12 maps and 12 charts (Govt. Press, Nagpur, 1914) by the late Lt.-Col. W. H. KENRICK, I.M.S., is one of the most important official documents on malaria published in India in modern times.[1] It has not received the attention it deserves. It is a most thoughtful and accurate record of a mass of facts collected with much skill and knowledge of detail. The investigation deals with 95,577 children, and malaria in rice-growing areas is specially considered. By examination of 30,000 children the rice-producing area in question is divided into three sanitary categories: (1) A healthy one comprising nearly the whole of the open plains country with a spleen rate among 12,384 children averaging 4·8; (2) endemic areas comprising the edges of the open plains and certain cultivated areas, all characterised by nearness to forest, jungle or hill, with a spleen rate among 9,075 children averaging 24·1, but ranging between 10 and 50, (3) hyperendemic areas with jungle and hill in excess and close to villages, and a spleen rate in 8,071 children averaging 70·5. In 100 blood films all species of parasites were found, the quartan being particularly associated with considerable enlargement of the spleen in endemic areas. Intensive cultivation of rice is not, then, here associated with malaria.

The commonest Anopheles is *A. fuliginosus*, *A. culicifacies*, the next, is held to be probably the main malaria carrier, since it was the only species (2 of 675 dissected) which showed sporozoites in the salivary glands, and corresponded in distribution with the malarial areas even when these comprised certain wards only of a town. Mosquitoes dissected numbered 1,052.[2]

2

THE RÔLE OF *A. ROSSII* AS "CARRIER" OF MALARIA: "THE *ROSSII*" PROBLEM[3]

(See p. 106)

Myz. rossii Giles [a synonym of *A. subpictus*] is widely distributed throughout India, Ceylon, the Andamans, Federated Malay States, Malay Archipelago, South China and the Philippine Islands The closely related species *A. vagus* Donitz (*A. rossii indefinata*) is found in Bengal, Assam, Burma, F.M.S. and Malay Archipelago, while *A. ludlowii*, which so recently as 1914 was regarded by BARBER and by SCHUFFNER as identical with *A. rossii*, is present in Burma, the Andamans, Madras, Ceylon and, predominantly, in the F.M.S. and the Malay Archipelago Only, then,

[1] It is only lately that the importance and comprehensive nature of this Report have been recognised

[2] *Trop. Dis. Bull.*, Vol 23, No. 2, February 1926, pp. 131, 132, abstract by Lt.-Col. CLAYTON LANE, I.M.S

[3] By Lt.-Col. C A. GILL, I.M.S., in the *Ind. Jour. Med. Res*, 1925, April, Vol. XII, No. 4, pp. 773–81 Abstract from *Trop. Dis. Bull.*, Vol. 23, No. 2, February 1926, p. 132, by Lt.-Col CLAYTON LANE, I.M.S.

in North-West India is *A. rossii* found alone. Is it in nature a conveyer of malaria? The belief of Indian malariologists is that it is not. This was tested by examining the insect in the Punjab in relation to these four postulates.—(1) Abundant presence corresponding to the malarial season. It abounds from July to November, which is precisely the main malarial season, and it so outnumbers the other species that, even if a feeble carrier, it must be harmful. (2) Capacity for experimental infection. Of 31 specimens fed on *P. vivax* blood 22 were dissected and 4 found infected with sporozoites. For *P. falciparum* the corresponding figures were 88, 67 and 0. *A. stephensi* used as controls were readily infected by both Plasmodia (3) Avidity for human blood. The mosquito being so readily found in stables the question of zootropism arose. It was, however, found to feed readily on man in nature, and in the laboratory; while serological tests showed that insects caught both in stables and habitations contained human blood. (4) Suitability of environment. Observations, described as incomplete, suggest that *A. rossii* is highly susceptible to low degrees of relative humidity.

"It would appear that the observations recorded in this paper tend to increase . . the obscurity surrounding the *rossii* problem," and it is noted that "if *A. rossii* be capable of transmitting *P. vivax* only, its prevalence when *P. falciparum* is epidemic might explain its taking no part in spreading malaria in the Punjab."

3

BIONOMICS OF MOSQUITOES

(See pp. 117–130)

The following highly interesting retrospect regarding the bionomics of Anopheles[1] by Lt.-Col. A. ALCOCK, C.I.E., M.D., F.R.S., I.M.S., will be useful to those engaged in original field investigations.

"In the control of Anopheles the study of the watery medium of the larvæ has recently come in for a good deal of careful attention. This also may be regarded as a subtle aspect of the organic environment, since (within the normal limitations of animal life) it can hardly be supposed that small variations in the physical and chemical characters of the water act directly and wholly upon the larvæ; it is much more probable that they act upon the microcosmic nutritional environment—upon the microscopic elements of that vegetable pabulum upon which the whole animal world is ultimately dependent MALCOLM WATSON, who drew attention to this subject many years ago, has again (1921) insisted on its practical interest. That it has a real practical interest in tropical rural areas must be obvious to all who have observed the results of trying to breed Anopheles larvæ, in bulk, in a laboratory where daily supplies of their own natural water are not obtainable. That the frequency of failure is not due to decomposition going on in the water is shown by the observations of HAROLD (1923), who bred *A. maculipennis* in water that stank. That failure is due to starvation and not to the obvious state of the water is the inference from the experience of that accomplished naturalist W. A. LAMBORN, who informed the reviewer that in Malaya he could rear every species of Anopheles with the one proviso that the larvæ were supplied with the common green Euglena. BOYD also (1926) has indicated the facility with which Anopheles larvæ are reared when supplied with yeast RUDOLFS (1924) also, who observed that water from claypits, containing high amounts of aluminium and iron sulphates, is inhibitive, concludes that it is the food of the larvæ that is affected by the chemical composition of the water. In the search for some over-mastering influence upon the natural conditions of life for Anopheles larvæ MACGREGOR (1921, 1924) has been attending to the pH reaction of the water. CABALLERO seems to have been too hasty in his conclusion that the cosmopolitan water-weeds of the genus Chara possess this interdictive influence, since numerous observers in various parts of the world find Chara and Anopheles larvæ happily associated—see in particular the papers of FISHER (1922), HACKER (1922), MACGREGOR (1924), and BARBER (1924) From BARBER's careful observations with *Chara robbinsii*, in Louisiana, it appears

[1] Abstract from *Trop. Dis. Bull.*, Vol 23, No. 7, July 1926, pp. 2–4.

that this species grows in thick mats in stagnant waters where larvæ of the local species of *Anopheles are extremely plentiful.* BARBER's laboratory experiments indicate the narrow limitations of the Chara doctrine; although in the laboratory the larvæ did not thrive along with entirely fresh green *Chara robbinsii,* they flourished if they were supplied with food, even if that food were finely-ground or rotting Chara. Another plant recently reported by WEED (1924) to have a deterrent effect upon Anopheles breeding is the ubiquitous water-hyacinth, here the explanation is that it gives specially good harbourage to the small Entomostraca, which feed on the eggs and small larvæ Still another kind of plant that has been fetched into the limelight is the modest bladder-wort, Utricularia, the bladder-like air-floats of which, as everyone knows, entrap and digest insects; BRUMPT (1925) and Langeron (1925) seem to think that even this humble aid is not to be despised in the struggle against Anopheles.

"The healthy persistence of species of Anopheles known to be susceptible to malaria in countries where endemic malaria—once extremely common—has practically disappeared is a good example of the 'excommunication' of a noxious insect from human intercourse by the creation of a sanitary environment for man. ROUBAUD explained this anophelism *sans* malaria as a change not only in the habits, but also in the structure of the maxillæ of the female Anopheles, due to the increase of stalled cattle; but the experiments of BULL & KING (1923), BULL & ROOT (1923), BARBER & REYNOLDS (1924) and BARBER & HAYNE (1924*a*), to name only these, do not support ROUBAUD's contention that the female Anopheles has a strongly marked special predilection for domestic animals. The reviewer's own observations (1925) of a well-spaced and well-housed population of a well-drained and well-farmed English district, from which endemic malaria has recently disappeared although Anopheles continues to thrive there, have led him to the conclusion that the Anopheles has been driven from human dwellings there by a modern sanitary environment, but still persists in large numbers outside that environment because there are plenty of farm animals to feed upon. The observations of NECHELES (1925) that it is atmospheric moisture that most influences the survival of Anopheles when they shelter in houses rather countenance this opinion. FALLERONI also (1924), though he believes that domestic animals have an actual protective influence against Anopheles, emphasizes the results of all that is implied in good farming. Before leaving the subject of Anopheles attention is due to experimental observations of BARBER & HAYNE (1924*b*), which are of general interest, on the dispersal and powers of flight of *A. crucians* and *quadrimaculatus.* In respect of flight also FISHER (1922) has noted distances of 2 miles and more, in Panama; and KLIGLER (1924), in Palestine, of more than 3 miles. A few remarks may also be made on the strange breeding-places of mosquitoes (including two species of Anopheles) in the crowns of cocoanut palms, described by HAWORTH (1924): but *that that author is confident in the truthfulness and trustiness of his native collectors* the association of a varied aquatic fauna with these mosquito larvæ would be regarded with mistrust. Workers wishing to breed successive generations of Anopheles in the laboratory should consult the papers of HAROLD (1923) and MARTINI (1925). CHRISTOPHERS's (1924) catalogue of the *Anophelini of the World* is a valuable work of reference."

(ii) EPIDEMIOLOGICAL RESULTS OF A LABORATORY STUDY OF MALARIA IN ENGLAND (*Trans. Roy. Soc. Trop Med. and Hyg.*, 1926, Vol. XX, No. 3, pp. 143–57).[1]

REPORT ON THE FIRST RESULTS OF LABORATORY WORK ON MALARIA IN ENGLAND,[2] *League of Nations Health Organisation.*

(See pp. 136–189)

The writer expresses his indebtedness to the Staff of the Bureau of Hygiene and Tropical Medicine for permission to reproduce the abstract of these two important and valuable reports of laboratory malaria work in England.

"An exhibited stereophotomicrograph of the spirochætes of syphilis in the aorta

[1] By Lt.-Col S. P. JAMES, I.M.S

[2] By Lt.-Col S. P. JAMES, I.M.S., assisted by P. G. SHUTE, 30 pp, 1926, Geneva. Abstract of both these communications in *Trop. Dis. Bull.*, Vol 23, No. 11, November 1926, pp. 804–6, by Lt.-Col. CLAYTON LANE, I.M.S.

of a patient suffering from general paralysis showed how indefensible might be the injection of such blood into other patients. Accordingly in England the official arrangement is that malarial infection, used in the treatment of this disease, shall be carried through mosquitoes. The infective agent was *Anopheles maculipennis*, the malaria parasite *Plasmodium vivax* of two strains, one from India, one from Madagascar. About 3,200 female *A. maculipennis* were collected in the adult stage from a country district where there was no malaria and used in 22 batches. Having been fed on one or more gametocyte carriers they were incubated at 22° to 24° C. in a saturated atmosphere till infective and then kept till required in an ice chest at temperatures of 4° to 6° C.

"The following facts have emerged Under these presumably favourable and sheltered conditions of incubation, the anopheline mortality is about 50 per cent. per week, so that, of 3,200, only 715 survived to infectivity. Only a small proportion of persons suffering from malaria are infective to mosquitoes. Gametocytes have never been found in thin films before the 7th day after the first rise in temperature, and about 3 days more elapse before they will infect mosquitoes. Their number rises rapidly, usually reaching a maximum about the second week of illness. More importance is, however, laid upon their 'quality' than their quantity, since there have been many failures when their numbers have been in excess of the often-quoted figure of 12 per cmm. of blood Their numbers vary extraordinarily, increasing for example in one case from 7 to 700 per 500 leucocytes; and females have outnumbered males. The infection of *A. maculipennis* after one feed upon an infective case is quite uncertain, and unless the quality of gametocytes is such that their host is an 'exceptionally good infector of anopheles' several feeds are necessary to secure a 100 per cent. infection of a batch. This seems to be due in part to the influence of the mosquito's food, certain parts of the blood of certain animals and birds rendering the stomach unsuitable for oocyst formation. Again, oocysts may form and die, the sporozoite stage never being reached, so that the finding of oocysts is no evidence that a mosquito [and presumably a mosquito species] may become infective. Further, in mosquitoes carrying nearly ripe eggs, the swollen ovaries prevent blood from entering the midgut and the mosquito from becoming infective, although in this case the œsophageal diverticula may be ballooned and give a false impression of probable infectivity. Similarly, individual greediness is a potent factor in determining the quantity of blood imbibed, though when gluttony pushes this to the extent of immediate evacuation it will operate against the likelihood of infectivity. 'The difficulties which have had to be overcome in order to obtain supplies of mosquitoes with 100 per cent. sporozoite infection of the glands have helped us to realize how many special conditions must be fulfilled in nature for the effective transmission of malaria from man to mosquitoes.'

"Infectivity having been acquired may be very persistent, surviving, for example, during three weeks at temperatures between 4° and 5 5° C. and during six days when it is below 0° C.; mosquitoes have remained infective from 20 to 92 days, so that taken with the findings of SWELLENGREBEL (*Trop. Dis. Bull.*, Vol. 22, p. 397), WENYON (Vol. 19, p. 277) and SELLA (Vol. 17, p. 147) 'we do not doubt that *P. vivax* can be carried through even a severe winter in hibernating mosquitoes, and that the carriage may be in either the oocyst stage or the sporozoite stage of the parasite or both.'

"Experiments showed that persistence of infectivity, when numerous opportunities of feeding were given, depended largely on continued reinfections. In passing on infection to man, 52 of 221 persons failed to develop malaria within the usual incubation period, and 50 of these failures occurred between November and March Yet during these winter months patients kept in bed in a warm room during the incubation period developed malaria, while others working in the fields did not. These failures to infect could not be explained on technical grounds, and so are referable to biological differences. Three types of susceptibility to infection are illustrated by cases.

"A case of normal susceptibility: bitten in July by 35 and by 8 infected mosquitoes, developing quotidian and tertian rigors, treated by 2 gm. [30 gr] of quinine daily for 5 days, reinfected by 120 mosquitoes a month later, developing 10 tertian rigors and, *after repetition of the treatment, remaining free from malaria (8 months)*. A case of supersensibility: bitten in August by 60 infected mosquitoes, showing 12 severe quotidian rigors, treated as above, relapsing six times, each relapse being treated in

the same way. A case of refractory type: bitten in December, February and April by 7, 9, 14 and 7 infected insects, showing 5 quotidian rigors, these disappearing without treatment, and the patient remaining well to date (3 months) without any quinine.

"Applying this experience to war cases, it is held that of the many thousands of malarial infections a certain number were of the supersensitive type and that these furnished the relapses seen in England. It is considered, then, that in a malarious place a few only of the vast numbers of anopheles become transmitters of malaria, and they do so because they happen to pass their life in an environment and manner very different to the others. After their first feed they become overloaded with blood and will fly but a few feet to some sheltered nook, whence they emerge nightly to feed and in time to infect or reinfect the household. The house, then, is the place where they must be sought and destroyed.

"In discussion Colonel CLAYTON LANE referred to the analogous condition noted by Dr. MANSON-BAHR as being produced in *Stegomyia pseudoscutellaris* by *F. bancrofti* in Fiji, where a heavy infection sickened and killed the mosquito, so that a heavily infected human case was a smaller risk to the community than a light one, and asked whether there was any evidence that malarial infection killed more mosquitoes than died when fed on non-malarial blood. He noted that no Italian 'bonification' was held complete without satisfactory housing. Dr. HANSCHELL urged the use of the household mosquito trap which he had found effective for mosquitoes in Barbadoes, where, however, Anopheles did not occur, and of the household larval trap which the late Dr. COGHILL instituted and used most effectively in Lagos in 1913. This consists of a tray containing weak copper sulphate solution, in which mosquitoes oviposit but in which larvæ die for lack of food. Colonel GILL held that the supersensitive case was the rule in India, and noted his failure to find any method of estimating the dose of sporozoites owing to the varying individual infectivity of any infected batch. In his experience, measured by their longevity, there was no disability to mosquitoes in India with malarial infection, and he questioned whether the house played an important part in infection in the tropics. Dr. STANNUS, without encouraging this means of protection, knew a number of men who drank two bottles of whisky a day and had had no malaria over a period of many years. Sir ALMROTH WRIGHT detailed the many fallacies which are inherent in such statistics as those dealing with the effect of malaria upon general paralysis and offered help in the physiological problems concerned. Dr. RUDOLF, referring to refractoriness to infection and the finding of Dr. MARSH that blood sugar decreased during malarial fever, suggested that it might be a matter of glucose content of blood. He emphasized that one who contrasted the discharges from Claybury Hospital of paralytics treated by malaria with conditions before this treatment could not question its effect. Dr. BALFOUR pointed out that all these paralytics must have had arsenicals, and that too little attention seemed to have been paid to that point in considering the striking effect of quinine on the malaria of these cases. The pH content of the mosquito's stomach might be a matter of importance. In reply Colonel JAMES stressed the reasons which had led the Malaria Commission of the League of Nations to advise that in the European countries which they visited it would be best to deal with endemic malaria by measures limited to affected individuals and to the interiors of the houses in which they lived."

(iii) PHYSICAL FACTORS IN MOSQUITO ECOLOGY

(See p. 130)

With the kind permission of the Editors of the *Trop. Dis. Bull.*, the writer reproduces Lt.-Col. A. ALCOCK's summary[1] of RONALD SENIOR-WHITE's article in the *Bull. Entom. Res.* of January 1926, Vol. XVI, Part 3, pp. 187–248, on the abovenamed subject. This abstract is necessarily condensed. Those investigating the bionomics of mosquitoes should read the original paper.

"It is many years now since MALCOLM WATSON suspected that it is something in the water itself rather than in its gross physiographical environment that determines

[1] *Trop. Dis. Bull.*, Vol. 23, No. 9, September 1926, pp. 207, 208.

its fitness as a breeding-medium for Anopheles, and thence hinted at the possibility of finding some means of controlling that insect simpler and less costly than drainage or than continual oiling. Later on LAMBORN took up the wondrous tale, and then MACGREGOR showed how Anopheles larvæ could be wrecked by a change in the pH concentration of the water and by the homely operations of the *dhobi*. The present author has approached this fascinating subject with all the apparatus of exact measurement, and he gives us here the results of a year's continuous and laborious study of mosquito-breeding waters in Ceylon. In the course of hundreds of observations he has collected an enormous volume of most interesting details, which, however, it is impossible to summarize, though the method and scope of his investigations may be noticed for the guidance of other workers.

"The first set of facts to be determined, as regards both natural and artificial waters, was the exact extent of toleration, by the mosquito larvæ living in them, of pH concentration and of total dissolved solids, oxygen, and saline ammonia—the important factor of albuminoid ammonia not being included in the survey. Since these combined factors may be assumed to act more directly on the vegetable organisms upon which the larvæ feed than upon the larvæ themselves, another matter of great interest was to make—as was made—a comprehensive survey, with specific determinations, of the algæ inhabiting the observed waters. Then the various natural phenomena known or inferred to be detrimental to the life of larvæ were observed and considered. Finally, some typical bodies of water were kept under periodic observation for a year, so that the seasonal play of the factors under study might be watched, and the associations of particular species observed.

"The following are some of the main conclusions: In Ceylon mosquito larvæ in general are found only between pH 5·8 and 8·6, species living in moving water having a wider tolerance than those in standing water—the former into acidity, the latter into alkalinity—and anophelines a wider tolerance than culicines. Natural-water-breeders are intolerant of any acidity not caused by CO_2. [The 'total' solids in solution were measured in terms of electrical conductivity, and are so expressed; but the limits, even in natural waters, appear—as indeed they do to common observation—to be extensive, i.e., from 62–922.] Waters in which dissolved oxygen is low are not favoured by Anopheles; for instance, *Anopheles listonii*, the only malaria-carrier commonly breeding in ricefields in Ceylon, was found to be dependent on a considerable amount of oxygen. *Saline* ammonia in amounts of less than 1 per million in natural waters was found to be inhibitory, especially to anophelines. A 'feeding-association' of certain mosquitoes, mainly anophelines, with certain algæ was observed, in other words, certain species are commonly found in association."

4

THE OCCURRENCE OF SEXUAL FORMS OF *PLASMODIUM FALCIPARUM* IN THE PERIPHERAL CIRCULATION [1]

(See pp. 169–171)

This valuable communication includes important data collected from many observations.

"In 1,789 thick film examinations of all fever cases among prisoners, made as soon as fever appeared, the monthly percentage showing crescents from July to February was respectively 4·8, 3·4, 0·5, 0·9, 10·3, 6·1, 4·4, 0·0. In 5,886 re-examinations of these men after treatment, the corresponding figures were 4·2, 2·0, 1·25, 1·25, 2, 17·2, 8·2, 1·1, 0. There is then a seasonal increase in crescent carriers in November in Lahore, Punjab, India. The sharp rise in November, and not earlier, may, however, need correlation with the fact that 'prophylactic quinine' was given once weekly during September and October to all prisoners who were not under treatment or under observation after treatment. The percentage of crescent carriers (equally with that of albuminuria) varies with the number of examinations made; for example, in 17,789

[1] J. A. SINTON, assisted by J. D. BAILY, and DIWAN CHAND, *Ind. Jour. Med. Res.*, 1926, April, Vol. 13, No. 4, pp. 895–916. Abstract from *Trop. Dis. Bull.*, Vol. 23, No. 11, November 1926, pp. 813, 814, by Lt.-Col. CLAYTON LANE, I.M.S.

Indians 4·25 per cent. showed crescents on the first examination; in 607 of these examined on numerous subsequent occasions this figure rose to 34·2. But this is not all the story, for the first examinations took place immediately fever began; crescents are not seen until 5 to 10 days after a febrile attack. It was found that in treated cases crescents became proportionately more numerous in those who had harboured many asexual parasites than in the opposite condition, though here again the question of detection in sparse infection has to be faced. The matter is put thus. DARLING showed that 12 gametocytes per cmm. of blood were necessary to produce infection in a mosquito; Ross has calculated that, using a thin film, the examination period for 1/12 cmm. is 1 hour; most workers employ 15 to 20 minutes; accordingly many infective carriers must be missed. The thick film uses 16 to 20 times as much blood as the thin, so that 1/12 cmm. will be examined in 3 or 4 minutes and even a single crescent is unlikely to be overlooked.

"The production of crescents is then considered. It is pointed out that BUCHANAN and THOMSON, as well as SINTON's own records, show that crescents develop when asexual forms are plentiful in the blood. It has been shown by many that they mainly develop in the bone marrow, much less frequently in the spleen. The reaction of circulating blood is pH 7·4. Rous has shown that certain actively metabolic organs, including the spleen, are 'acid organs' and it is suggested that stagnant backwaters like the spleen and bone marrow will be more acid, though no evidence regarding the latter is offered. An interesting observation is mentioned. A culture of *P. falciparum* was overlooked for 10 days in an incubator, and when examined was found to contain large numbers of crescents and no asexual forms—although no crescents had been found in the patient's blood nor in the culture during the 72 hours in which it was examined. The point is to be further elucidated in connection with the hydrogen-ion concentration; since SINTON and BAILY have found a lowered alkali reserve during acute attacks of subtertian malaria, and crescents appear in maximum numbers about 10 days after such a paroxysm. No correlation was found between splenic enlargement and crescents. The life span of a crescent is considered. If crescents be formed from asexual forms, and if asexual forms be killed by quinine, then the further formation of crescents will thus be prevented and the life span of those present will be the measure of the normal life span of the crescent, provided, as seems to be the case, these are unaffected by quinine. This point was determined by treating 501 cases with quinine for 4 to 7 days and observing them weekly for 8 weeks. The percentage found harbouring crescents before, during and after the 8 weeks was 6·9, 25·2, 15·0, 8·5, 3·7, 2, 0·7, 0·3, 0·3, 0. It is concluded that, while the life span may reach to 60 days, it is ordinarily 30.

"'The presence of crescents after the finish of treatment cannot, therefore, be taken as evidence that the treatment has not cured the infection, unless one believes in the parthenogenetic theory of relapse, which does not seem to be supported by our results, for, in spite of the fact that no treatment was given during the observation period, no relapse was recorded among 127 of the patients who showed crescents in their blood, even although the majority of these patients were examined weekly for at least five weeks after the crescents could no longer be found.'

"It is held that the quinine and alkali treatment [*see* p. 255] gives better results in preventing the formation of crescents than does other treatment, and concluded that, as a practical measure, isolation should continue for 3 weeks after cessation of that treatment."

5
FORMS OF MALARIA PARASITE
(*See* pp. 172, 173)

Many morphological variations of malaria Plasmodia have been described and depicted, but it is now almost universally accepted that only three distinct species exist as parasites of man throughout the world. "The publication in 1914 by J. W. W. STEPHENS of a new species of malaria parasite under the name of *Plasmodium tenue* occasioned considerable comment amongst malariologists." The main claims of *P. tenue* to a distinctive name were "the marked amœboid forms, the large size of

the nuclear chromatin and the irregularity in shape of the schizonts. A. BALFOUR and C. M. WENYON pointed out (1914) that such distinctive forms were not uncommon in *falciparum* infections. In the October 1926 issue of the *Kenya Medical Journal*, J. C. J. CALLANAN shows, by means of three excellent plates of camera lucida drawings, that *tenue* forms of the parasite can be demonstrated in the same preparations as ordinary ring forms of the subtertian parasite, and that the former are found only in distorted red blood corpuscles which have been subjected to pressure, none being demonstrable in those portions of the blood slide where the cells are superimposed. That *tenue* forms are indeed artefacts is conclusively proved by their absence from fresh preparations of subtertian malarial blood In *tenue* cases which came to autopsy, preparations from the brain and spleen invariably showed parasites identical with *falciparum* In blood films in which too great pressure has been exerted in their preparation the majority of the *tenue* forms lie in one general direction, at right angles to the edge of the film." [1]

STEPHENS,[2] however, while agreeing that the shape of malarial rings differs with their position on the slide, is of opinion that CALLANAN was not dealing with *Plasmodium tenue*, since the latter's drawings are nothing like the specimens of that parasite in STEPHENS's possession. CALLANAN described a structure quite different from STEPHENS's *tenue*. In the discussion, to which Prof. STEPHENS's remarks were a reply, Major J. A. SINTON correlated geographically *tenue* forms with blackwater fever, particularly in India.

6

DIAGNOSIS OF MALARIA

(See p. 195)

A blood sedimentation test for the diagnosis of malaria from kala-azar, enteric and other fevers has recently been described in a preliminary note by Lt.-Col. E. C. HODGSON, I.M.S., A. C. VARDON and ZORAWAR SINGH.[3] It is stated to be a quick and simple means of differentiating malaria from the diseases named.

7

HÆMOGLOBINURIA, AND JAUNDICE *SINE* HÆMOGLOBINURIA FOLLOWING QUININE TREATMENT OF MALARIA [4]

(See p. 205)

The relationship between quinine treatment of malaria and its production of hæmoglobinuria has been dealt with by many authorities on malaria. Among the more recent essays on the subject are the 103 cases collected by Prof. J. W. W. STEPHENS and H. STOTT (1915),[5] which show an intimate connexion between the administration of quinine and hæmoglobinuria. J. GORDON THOMSON [6] (1924) published two striking cases showing the correlation. It would seem that "while quinine in many cases does not play a leading part in the genesis of hæmoglobinuria, cases do occur in which it seems to act definitely as the immediate cause." The way in which the quinine precipitates the attack is not as yet definitely known ; the subject is briefly alluded to on p. 206: "It is generally accepted that the hæmoglobinuria is secondary to a hæmoglobinæmia brought about by the lysis of erythrocytes in the blood stream." This view of intravascular hæmolysis is indirectly supported by certain observations.

"It is now generally accepted that hæmoglobin is broken down in the cells of the reticulo-endothelial system, particularly, if not wholly, by the Kupffer cells which are

[1] *The Lancet*, Editorial Note, January 8, 1927, p. 91.
[2] *Trans. Roy. Soc Trop. Med. and Hyg*, 1927, Vol. XX, p. 420.
[3] *Ind. Jour. Med. Res*, Vol XIV, No 3, January 1927.
[4] G. R Ross, M B, Ch.B, Ph.D., and G H. PEALL, M B, B.S. Lond., F.R.C.S. Ed, in the *Brit. Med Jour.*, January 8, 1927, pp 53, 54.
[5] *Annals of Trop. Med and Paras.*, Vol 9, No. 1, p. 201
[6] London School of Trop. Med. Res. Memoir Series, Vol. VI, *Researches in Blackwater Fever in S. Rhodesia*, p. 86

found in the liver sinuses, and is converted into bilirubin and hæmosiderin. Thus, in conditions in which hæmolysis exists, an increased output of bilirubin can be anticipated. That this is the case in malaria, in which blood destruction in excess of normal exists, has been shown by van den BERGH (1924), HUGHES (1924), and KINGSBURY (1926). Van den BERGH'S test is now so widely employed that it requires no description, but it may be emphasized that not only does it afford a measurement of the amount of bilirubin present but it also distinguishes between what might be termed mature and immature bilirubin in the serum. Mature bilirubin is that which has passed through the polygonal cells of the liver and has then been absorbed into the blood stream, and is present in cases of obstructive jaundice. This variety gives the direct reaction. If, however, owing to rapid blood destruction, bilirubin is produced at so rapid a rate that the polygonal cells are unable to deal with it *in toto*, the excess is absorbed directly into the blood stream from the Kupffer cells, and forms the immature bilirubin which gives the indirect reaction. An indirect reaction should, then, be obtained in those cases where the pathological factor is increased blood destruction, and it is this variety which occurs in pernicious anæmia and malaria. Such a reaction can be accepted as evidence of intravascular hæmolysis.

"In hæmoglobinuric fever, in the initial stages of the disease, the indirect reaction is strongly positive and the number of units of bilirubin present shows a huge increase on the normal amount of 0·2 to 0·5 unit found in normal controls (unpublished results of one of us, G. R. R.). We have thus indirect evidence that hæmoglobinuria in hæmoglobinuric fever is accompanied by hæmoglobinæmia. There can be no doubt that the hæmoglobinæmia must precede the hæmoglobinuria. Assuming, then, that hæmoglobinæmia exists, it can be postulated that two mechanisms at least come into play in the endeavour to rid the body of the hæmoglobin dissolved in the plasma. At first there is an increase in the activity of the reticulo-endothelial system, so that as much as possible of the hæmoglobin may be disposed of by the normal methods of converting it into bilirubin. This we know does happen. If, however, the amount of hæmoglobin is in excess of the maximum with which the reticulo-endothelial system can deal, then excretion by the kidneys occurs, with consequent hæmoglobinuria. We can thus assume that there exists a threshold value for hæmoglobin ; whether that is constant or whether it varies from individual to individual is not as yet clear. It cannot be assumed at present that the reticulo-endothelial system, on the activity of which the threshold value must in part depend, functions equally in every individual. It is, however, known that if the hæmolysis be slow and gradual, as in pernicious anæmia, or even sudden but relatively slight, as in malaria, hæmoglobin does not appear in the urine.

"Turning now to the question of quinine hæmolysis *in vivo*, it is conceivable that if quinine can produce hæmolysis sufficient to cause the appearance of hæmoglobin in the urine, cases might occur in which the degree of hæmolysis is so slight that the free hæmoglobin can be disposed of entirely by the reticulo-endothelial system without the appearance of hæmoglobinuria. References to this possibility are relatively few. KOCH (1898) stated that after the administration of quinine an attack of icterus may occur. BLACKLOCK (1923) believes that hæmolysis with slight jaundice can occur without hæmoglobinuria and that this condition is frequently due to the same cause as blackwater fever."[1]

ROSS and PEALL follow the above remarks with the details of a case of icterus with no accompanying hæmoglobinuria after quinine treatment of malaria. "There can be no doubt that the jaundice was hæmolytic in type." In this case the dosage of quinine was very small, only 1½ grains were given daily and only 51½ grains had been administered altogether when the jaundice became clinically apparent."

The author is familiar with these cases of jaundice without hæmoglobinuria during the quinine treatment of subtertian fever in India, and noted that it has various degrees of intensity, and, over thirty years ago, observed that discontinuance of the quinine brought about the disappearance of the jaundice.

[1] ROSS and PEALL in the *Brit. Med. Jour.*, January 8, 1927, pp. 53, 54.

8

PATHOLOGY OF MALARIAL SPLEENS AND EFFECTS OF RADIOTHERAPY ON THEM

(See p. 232)

P. HEYMANN [1] recognises two distinct types of malarial spleens—the acute and the chronic In the acute type, which follows a recent infection, the increase in the size of the organ is relatively small, the main lesion being a universal congestion of the adenoid elements, in the chronic, due to a slow infection lasting a long time, the spleen is greatly hypertrophied, often reaching the umbilicus and even invading the left hypochondrium. In these latter cases there is, " besides a congestion of the Malpighian follicles, a hypertrophic sclerosis, not only of the pulp, but also of the follicular portion."

P HEYMANN [2] reports sixteen cases of malarial splenomegaly treated by X-rays and describes the treatment in each of the three groups into which he divided the cases. " His findings were that in acute cases there was a complete regression, due to the influence of the rays on the lymphoid tissue, and in the chronic this diminution in size was only partial, the Malpighian follicles being affected by the rays, while the greater part of the spleen, being composed of fibrous tissue, was unaffected." He concludes that " radiotherapy is efficacious in certain acute cases, but that it does not bring about a complete amelioration in chronic ones where a profound fibrous infiltration renders the tumour insensible to the action of X-rays." He considers that the length of the treatment, its difficulties and inconveniences, justify rejection of this form of treatment of malarial spleens, that acute spleens regress spontaneously or with the aid of quinine and arsenic treatment, and that chronic cases are best relieved by surgery.

9

REMARKS ON THE PATHOLOGY OF MALARIA

(See p. 232)

Prof. A. BIGNAMI [3] published some remarks on the above-named subject from which the following abstract by Lt.-Col. CLAYTON LANE [4] is reproduced.

" It has been maintained that certain inflammatory lesions found in malaria must be of malarial origin because no other micro-organism has been found. Epidemic meningitis, it is pointed out, has this feature. The lesions of malaria, it is insisted, are not inflammatory; they are necrotic and proliferative. In the brain, for instance, round an arteriole blocked with parasites and pigment, lies a necrotic area surrounded by a ring of hæmorrhages from surrounding vessels. Such lesions may be found in the part of the brain where they would be expected from the symptoms during life. Tumours of liver and spleen are not inflammatory. An acutely enlarged liver shows: first, congestion with some necrosis of the parenchyma; then, a perilobular melanosis; by repetition of the process, some increase of interlobular tissue; on recovery, abstraction of pigment; in cachexia, atrophy from progressive anæmia. Inflammatory lesions, if present, can only be due to some cause other than malaria."

10

ANIMAL PROPHYLAXIS IN MALARIA [5]

(See p. 312)

In connexion with the screening of man from Anopheles by animals, M. O. T. IYENGAR divides these insects into four groups: "(1) Species essentially wild—*A. gigas*,

[1] Quoted by the *Brit. Med. Jour.*, Epitome of Current Medical Literature, February 5, 1927, p. 26

[2] *Jour. de Radiol et d'Electrol.*, November 1926, quoted as above.

[3] *Semana Médica*, 1926, February 25, pp. 424–6.

[4] *Trop. Dis Bull*, Vol 23, No. 7, July 1926, p. 554.

[5] M. O. T. IYENGAR, *Rep. Proc. Fifth Entom. Meeting, Pusa*, 1923, pp. 203–12.

barbirostris, aitkenii and *lindesaii* ; (2) species preferring animals to man—*A. hyrcanus* (sinensis), *fuliginosus, jamesii, maculipalpis* and *maculatus* ; (3) species preferring man to animals—*A. vagus, subpictus, jeyporiensis* and *culicifacies* ; (4) species living solely on human blood—*A. minimus, listonii, varuna* and *stephensi*."

II

LARVICIDAL EFFECTS OF PETROLEUM

(See pp. 313, 314)

In the *Fed. Mal States Bureau Reports*, 1925, Vol. 3, is published a thesis by H. P. HACKER which deals minutely with the appearances seen in larvæ killed by contact with oil, "with the effects of differential wetting of the larval structures on the position of the larva, on the mode of action of the oil," and other interesting points. The following are his general conclusions :[1]

"(1) Differential wetting has been shown to be an important factor in the life-history of larvæ, and in their susceptibility to the effects of oil.

"(2) Anopheline larvæ place themselves at right angles to a wet object because their tails are wet and their spiracles are dry. The larvæ lie parallel to a dry object because their dry spiracles are 'attracted.'

"Oil on the surface of water acts like a dry object and 'attracts' the spiracles. When contact takes place the oil is able to wet the spiracles and therefore enters the breathing tubes. Contact with oil is sufficient to kill larvæ, and the appearances shown by oil in the tubes have been described.

"(3) A 0·1 per cent. solution of soap is able to wet the spiracles so that the larvæ can no longer rest at the surface and ultimately drown.

"(4) Weak emulsions of oils do not enter the breathing tubes and kill larvæ unless there is a film of oil on the surface. Wet oil does not 'attract' the spiracles of larvæ.

"(5) The spread of oil and the movement of thymol particles depend on the affinity of water for active groups in the substance. Both may be prevented by satisfying this affinity by saturating the water with a material containing an active group.

"(6) Pure hydrocarbons do not spread on water. Oils that spread contain substances which have active groups, and these substances have an affinity for the oil on one hand and for water by means of their active groups on the other.

"If the oil contains too much active material the excess leaves the oil, satisfies the affinity of the water for active groups, and thereby prevents the oil from spreading.

"Crude oil has been shown to be a satisfactory mixture because it does not contain an excess. A method of testing whether any given mixture contains too much active material has been described.

"(7) Methods for comparing the spreading powers of oils have been suggested. One of these depends on the amount of oil which must be added to pure paraffin in order to make the mixture spread. The other is based on the extent to which inactivated water must be diluted with fresh water before the oil can spread.

"(8) The substances which cause spreading are increased by oxidation.

"(9) Pure hydrocarbons are able to wet the spiracles. They can thereby enter the breathing tubes to kill larvæ.

"Volatile hydrocarbons condense as a film on the lining of the breathing tubes and produce a pseudo-anæsthetic effect.

"This film increases the absorption of alcohols and thereby enhances their toxic action, which is a true anæsthesia.

"(10) The toxicity of kerosene is increased by oxidation in the same way as the spreading power. The toxicity and the spreading power are therefore probably due to the same substances."

[1] *Trop. Dis. Bull.*, Vol. 23, No. 12, December 1926, pp. 864, 866.

12

TOP MINNOWS AND MOSQUITO CONTROL[1]

(See pp. 322–327)

Various species of Gambusia have been used for consuming the larvæ and pupæ of mosquitoes for the last quarter of a century, but opinions have been widely divergent as to their efficacy in reducing the numerical prevalence of mosquitoes. This difference of opinion is specially marked in India. A brochure (*A Study of the Top Minnow*, Gambusia holbrooki, *in its Relation to Mosquito Control*) recently issued by the U.S. Public Health Service, if it does not convince the incredulous, at least indicates the necessity of a thorough investigation of the subject of fish control of mosquitoes in India. The bulletin under reference is replete with important and interesting facts, the data for which were largely derived from experimental work. Numerous experiments and controls were carried out. "Sections of ponds in various situations were rendered fishless, others under as nearly as possible the same surroundings were employed for control, so that the differences in the mosquito-breeding would result in the main from the presence or absence of fish. By carrying out the experiments for three or four seasons, and using ponds with different forms of vegetation, much knowledge has been gained as to the value of Gambusia as eradicators of mosquito larvæ and pupæ under a wide range of conditions. These fish had been found to vary in efficacy in different districts, being less efficient in the northern parts of their range. This is probably due, not to the district, as was believed, but to the species of Gambusia ; thus, *G. holbrooki* of Eastern Georgia differs in efficiency from the *G. affinis* of the Mississippi Delta region. After arranging the experimental and control conditions, as regards fish, vegetation, water-level, and so on, dippings (each 'dipping' = twenty-four dips with a net) were taken, and the relative abundance of mosquitoes breeding in the areas was calculated by counting the larvæ and pupæ recovered in each dip, anophelines and culicines being counted separately. The following are a few of the more important results and deductions. Silver-leaf grass, pond-weed, milfoil, bladderworts, smartweed, and several others tested each afford protection to the larvæ from the attacks of the fish, but not under all conditions. Thus, milfoil protects if it grows sufficiently tall to reach the water surface, not otherwise. Again, if on clearing an area some sprigs of silver-leaf grass were left here and there, a scattered growth soon formed, which afforded effective refuge to the immature mosquito, and thinning of the grass tended, paradoxically, to increase the available protection. The practical conclusion from this is that, from the point of view of mosquito control by fish, it is better not to disturb the natural growth of grass unless the latter is completely removed. Bladderwort had been reported by many observers as being antagonistic to mosquito production, but experiment failed to confirm this, and, moreover, if intermixed with filamentous algæ it appeared to conduce to the better breeding of mosquitoes by furnishing an excellent barrier between the fish and the larvæ and pupæ. It was found that when smartweed was present, even in the absence of fish, the larvæ were scarce. No complete explanation could be found for this ; the plant did not act as a repellent, for if the water-level fell sufficiently to leave the plant exposed, larvæ and pupæ became abundant. The only plant which proved definitely preventive to mosquito breeding was duckweed, and this was shown to be due, not to any specific action, but to the exuberance of its growth. If the weed was so profuse as to cover the surface breeding did not occur, but was resumed on clearing, to fall again when the weed was re-introduced ; to prevent breeding the covering must be continuous. Its use, however, is very limited, because it will not grow in all waters, and in some of those in which it does it will not form a continuous coat. Generally it was found that 'overstocking' with Gambusia, though leading to a little further reduction of larvæ and pupæ, had not a very pronounced effect, but beneficial results were sometimes obtained by artificially increasing the number of minnows in a body of

[1] The writer has to thank the Editor of the *British Medical Journal* for permission to use the editorial note under the above title which appeared in the issue of January 8, 1927. It is a review of *A Study of the Top Minnow* (Gambusia holbrooki) *in its Relation to Mosquito Control*, Public Health Bulletin No. 155, U S. Public Health Service, Washington, D.C.

water where they had been present for a long time, because a 'biological balance' is liable to become established and further reduction cease. After heavy rains a diminution in the breeding of mosquitoes was noticed in the ponds whether Gambusia was present or not. In the former case the minnows always seemed to be more active after rains, and the explanation given is that the increase of water caused submerging of the vegetation and consequent reduction of protection of the larvæ. This, however, would not account for reduction in fishless areas. It was found generally that the maximum protection was afforded by plants with partly or just submerged leaves, so that only a thin film of water was present in which the mosquitoes might breed. *Gambusia holbrooki*, which was the species used in these experiments, proved more efficient in eradicating culicines than anophelines Attempts were made to find out—obviously a very difficult problem—the proportionate number, in a pond well stocked with Gambusia, of immature mosquitoes present which reached the imago stage. As far as careful experiments could decide, it was found that only 2·75 per cent. of anophelines and 1·5 per cent. of culicines survived. It is important to note that absence or scanty breeding of mosquitoes is not always the result of the presence of natural enemies ; in some ponds, apparently ideal, they would not breed, although the conditions seemed to be in all respects—vegetation, situation, exposure, etc.—identical with others in which there were abundant larvæ. The subject is a large and important one, and this bulletin, full of interesting information, has done much to elucidate many problems hitherto obscure." [1]

The author has shown that it is unnecessary to import Gambusia for use in India (p. 326). There are many species of larvivorous fish in that country with which experiments corresponding to those mentioned above could be carried out.

[1] *Brit Med. Jour.*, Editorial Note, January 8, 1927, pp. 71, 72.

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